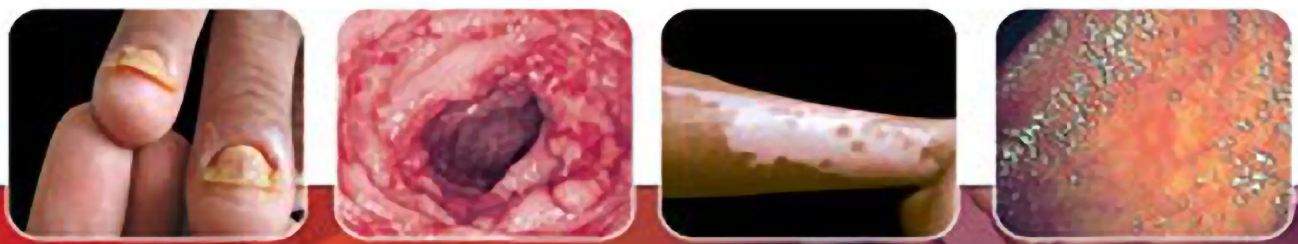
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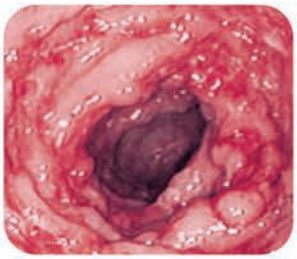
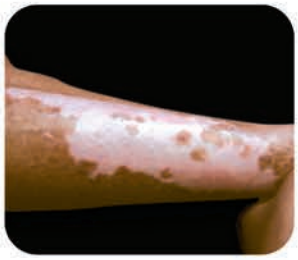
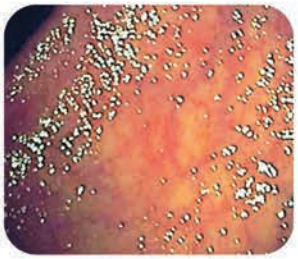
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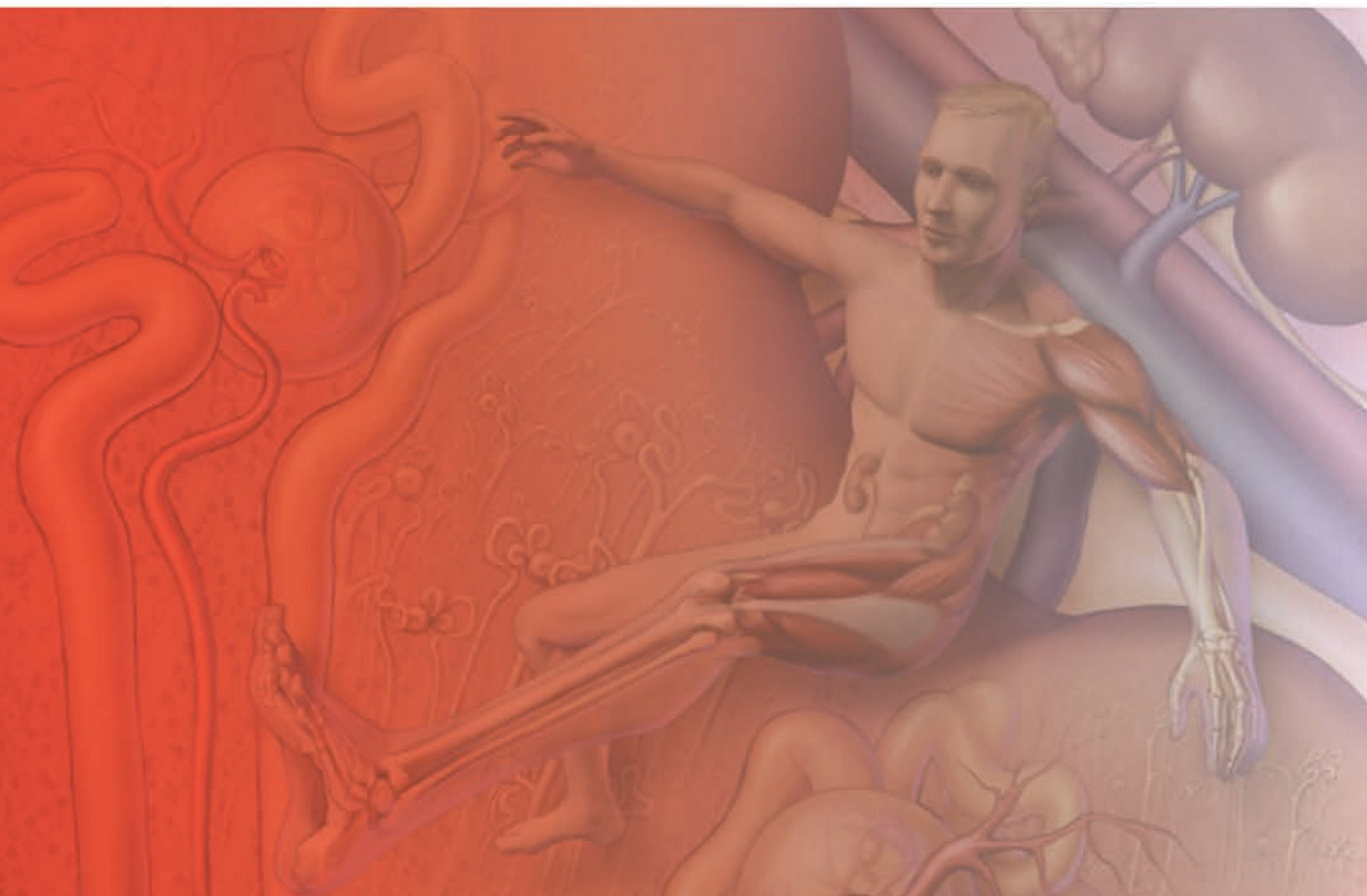
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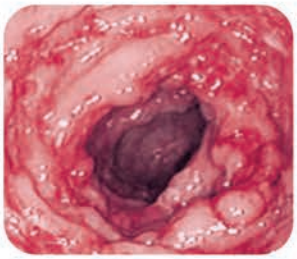
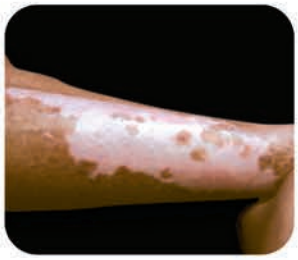
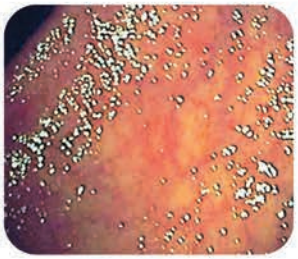
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Clinical Medicine

A Textbook of Clinical Methods and Laboratory Investigations



Fourth Edition

Clinical Medicine

A Textbook of Clinical Methods and Laboratory Investigations

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the memory of all patients who
entrusted their health and life to us
and
who have helped us to shape our
careers as physicians caring for them

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Preface to the Fourth Edition

There is great need for a textbook of clinical medicine for the use of medical students and practitioners, with due emphasis on the local conditions. Several books are available which are popular among students and teachers. All these books are highly informative and useful but emphasis is given to the conditions prevailing in their countries of origin.

The present medical scenario in addition to many of the diseases caused by poor socio-economic conditions, most of the diseases encountered in developed countries such as lifestyle-related diseases, diseases of advancing age and diseases caused by tobacco and biomass fuel smoke, disturbance in family relationships, road accidents, environmental changes, more migration to townships without adequate development of infrastructure; have all constituted to a change in disease patterns and epidemiology leading to gross change in the prevalence and pattern of diseases. There is considerable overall improvement in the financial, socioeconomic, educational and infrastructural improvement, but still vast areas of the country are deficient in infrastructure, clinical facilities and availability of appropriate modern medical care. Basic investigations such as simple laboratory tests, X-rays, electrocardiography (ECG) and even ultrasound studies are available in even remote villages and towns. There is a rapid proliferation of secondary care and tertiary care hospitals in the private sector, which provide health care on payment. These are available only to a smaller section of society.

The concept of primary care physician, which dominated till the middle of the twentieth century has given place to the era of specialists and highly skilled specialists, so that the first entrants into the medical studies proceed towards postgraduation and further acquisition of skills. Their services are available only in towns and cities, where most of the secondary and tertiary care private hospitals are located. The students and young physicians joining the medical profession have to be aware of these facts and it is their bounden duty to provide medical care to the less affluent masses too. This entails the proper acquisition of clinical skills, which alone may be adequate to diagnose and manage the vast majority of diseases occurring in the community. The doctor should use his discretion to plan the investigations which reduce cost and inconvenience to the patient. It is absolutely essential that cost-effective investigations have to be planned. All these require a thorough knowledge of the principles underlying clinical examination and the interpretation of investigations. Moreover, at the present time, when many young doctors may have to practice in remote communities single handed, many investigations have to be carried out by themselves, e.g. urine examination for glucose, acetone and deposits, examination of feces for ova of worms, or examine a blood smear for malarial parasites. The ECGs and skiagrams may have to be interpreted without help. To facilitate the establishment of such laboratory tests and empower the doctor to interpret the abnormalities, this book gives practical details to perform such simple tests. In the case of the more complicated tests, only the principles and interpretation of the findings are given.

The book is designed to provide information on complete clinical examination, correlation of clinical findings with pathological processes and guidance to select investigations in a cost-effective manner. This book is produced in two parts. *Part I* includes Clinical Examination and Investigations required for training in the general medical wards. *Part II* contains other medical disciplines included in the undergraduate curriculum—Pediatrics, Geriatrics, Pregnancy, Dermatology, Leprology and Sexually Transmitted Diseases, Psychiatry, Ophthalmology, Ear, Nose and Throat, Examination of Oral Mucosa and Teeth, Community Medicine and Statistics and Information Technology.

All the sections have been thoroughly revised and modified depending on the development in the subject so as to provide up-to-date information to the learner. Several photographs have been added to facilitate self-study by the students.

The book is intended also to cater the needs of undergraduates throughout their course, internship, further clinical studies, preparation for postgraduate entrance examinations in internal medicine and practitioners in India. The students of others systems of medicine and practitioners of alternate systems may also find the interpretation of physical findings and planning of investigations useful. The sections on Community Medicine and Statistics and Information Technology have been specially designed to help the students to read and understand modern medical literature, interpret published material critically and plan research at the basic level. The section on information technology is intended to make the reader aware of modern developments in this field and to acquaint himself to the use of tools to get further information.

All the contributors, who are veteran teachers, have tried their utmost to bring out the book as a useful companion for studying clinical medicine.

KV Krishna Das

Preface to the First Edition

There is great need for a textbook of clinical medicine for the use of medical students and practitioners, with due emphasis on the local conditions. At present, the vast majority of medical students depends on notes prepared during bedside clinics and supplemented by information obtained from books on clinical medicine. Though most of these books are highly informative and useful, emphasis is given to the conditions prevailing in their countries of origin. Many of them are written to cater to the young students who have access to advanced investigations at hand.

The situation is different from the economically developed countries. A large number of patients flock to the primary care physician. Facilities for investigations are limited due to the scarcity of services. The cost of investigations is high and also unaffordable by the patients at large. The physician, therefore, has to be very careful in planning investigations which are readily available in a cost-effective manner. Detailed clinical examination is absolutely necessary to achieve this end with the least expense while providing the greatest benefit and satisfaction to the patient.

Clinical methods have changed considerably depending on the changes in disease patterns and availability of investigative facilities. The situation is special. The clinical spectrum is a mixture of diseases seen in underdeveloped regions of the world such as malnutrition, infective diarrheas and tetanus plus those seen in higher proportion in advanced countries, such as diabetes, ischemic heart disease, hypertension and cancer. Facilities for basic investigations are available in many parts, but large areas of the country are devoid of them. In many cases, the primary care physician has to organize investigations. Specialist facilities and commercially oriented high-technolgoy medical institutions are springing up in many towns and cities. They mainly cater to the small affluent section of the population. These facilities are beyond the reach of large masses. Appropriate clinical methods will go a long way in providing medical care to larger sections of the population. This book is the result of attempts made in this direction, on the advice of my peers and colleagues, and request from numerous students and young physicians, who have found my *Short Textbook of Medicine* quite useful.

The book is designed to provide information on complete clinical examination, correlation of clinical findings with pathological processes and guidance to select investigations in a cost-effective manner. Investigations, which the medical student or physician have to perform are described elaborately. The book is produced in two parts. *Part I* includes Clinical Examination and Investigations required for training in the general medical wards. *Part II* contains other medical disciplines included in the undergraduate curriculum—Dermatology, Sexually Transmitted Diseases, Pediatrics, Obstetrics, Otorhinolaryngology, Ophthalmology and Psychiatry. A short section on Community Medicine and Statistical Methods is also included since these are most essential for the success of any primary health care physician. The use of computers in medicine has also been included to prepare the students for the future trends in medicine.

Compared to all other sections, section XI on Neurology is relatively longer and more exhaustive. This has been deliberately done in spite of the apparent disproportion between the sections because in all postgraduate clinical examinations, the main clinical long case is invariably a neurological problem. This is

so, since the elicitation of obvious findings, their interpretation and planning of investigations, etc. lend themselves for easier and more objective assessment. To the student, who has not understood clinical neurology well, these exercises are nightmares. At present, the available undergraduate books on clinical medicine deal with neurology in the same manner as the other sections, since these books cater to the undergraduates. As such, the student going for postgraduate examinations has to resort to monographs in neurology to acquire skills required of them in the clinical examinations.

The book is intented also to cater to the needs of postgraduates in internal medicine and, therefore, this section had to be made comparatively more exhaustive. I wish, it fulfils the need it is intended to provide.

KV Krishna Das

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My editorial committee members and all the contributors have spent much time in putting considerable effort to update the material, add newer chapters demanded by the students and teaching communities and increase the number of illustrations to make the book user-friendly and attractive. Late PK Mohan had assisted in writing of chapters 31 to 34 of Section 11 (Neurology). Close interaction of the members of the editorial committee and the contributors has helped to make the text up-to-date and attractive.

Mr Abraham Jacob, did the DTP work and put the illustrations in place. The encouragement, patience and endurance of my wife, Mrs LN Kamalam, went a long way in encouraging me to complete the editorial task in time. Dr S Anand (Associate Professor of Ophthalmology) read the proof of chapters in ophthalmology and did corrections.

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PART–I
Internal Medicine

SECTION

1

Clinical Medicine

CHAPTER

1

Clinical Medicine: An Overview, Patient History, Evidence-based Medicine and Diagnostic Test Evaluation

KV Krishna Das, C Sudheendra Ghosh

Patient identification, History, Environmental factors, Socioeconomic factors, Details of place of residence and recent travel, Addictions, Evidence-based medicine and diagnostic test evaluation

PATIENT IDENTIFICATION

It is important to make proper records so that the patient can be identified and recalled at a future date for follow-up. One of the serious handicaps in day-to-day practice is the want of a proper address and other details of identification of the patients so that many of them may be lost to follow up. Moreover, many patients change their addresses frequently so that the same person may be registered under different addresses in the same institution or different institutions. It is therefore, desirable to give the following details:

Name_____ Age_____ Sex_____

Residential address (present) _____

Permanent address_____

In case of those who do not have their own permanent houses, details of residence with reference to a school, post office, temple, or any other landmark may help to trace them out in future. While recording occupation, state the actual type of work, e.g. executive, technical person, manual laborer, etc. Since many diseases show close relationship to occupation, it is essential to give a brief description of the work done by the patient. Agricultural workers are more prone to develop helminthiasis, leptospirosis, and poisoning by pesticides. Workers in the carding and spinning areas of cotton mills are more exposed to cotton dust which provokes asthma.

It is desirable to include other details such as ethnic group and religion. It should be noted that in India the same ethnic groups profess different religions and therefore, classification based on religious faith may not reflect ethnic differences.

HISTORY

The doctor starts the first contact with patient during history-taking (interrogation). This is the first step which paves the way for a firm doctor- patient relationship, which is essential for mutual confidence and trust. Many parts of the history of the illness pertain to very close personal matters of the patient which he may not reveal to anyone other than a doctor. Therefore, strict privacy has to be maintained during interrogation. Matters revealed by the patient to the doctor have to be kept confidential and not be divulged to others except under certain special circumstances.

Of all the methods of examination, history-taking is the most important single method which gives maximum diagnostic clue. Most of the diseases follow a general pattern of onset, evolution and course, and therefore, a properly taken history gives diagnostic clues in many of them. It is important to spend time in eliciting the history of illness patiently, and record it in a sequential manner to reveal the pattern of disease. In over 50% of illnesses, the diagnosis can be arrived at by history alone, the physical examination and investigations help to confirm it. In the other half, history takes the doctor very near the diagnosis

but physical examination and investigations are absolutely necessary for the final outcome. As a general rule, the term "symptoms" is used to denote the complaints given by the patient and they represent the subjective experience of the patient. "Signs" denote the findings made out by the doctor on physical examination and they represent the objective evidence of disease. In many cases symptoms and signs overlap, for example, a patient may complain of an abdominal mass which the doctor also may detect on palpation.

Interrogation of the Patient

General Considerations

Whenever possible, the history should be taken directly from the patient. If the patient is unable to give the history (children, comatose patients, etc.) the attendant who has witnessed the illness has to be depended upon. The patient should give out the history spontaneously from the onset to the present condition, including all events such as exacerbations, complications and treatment obtained. As far as possible the spontaneous reporting by the patient should not be interrupted by the doctor, unless the latter is convinced that the patient is narrating irrelevant matters on the belief that these are his genuine complaints. Leading questions should be avoided during the spontaneous narration of the history by the patient since leading questions from the doctor which suggest the answer may make the patient reply in the affirmative, and this may mislead the doctor. After the patient has finished narration of the total history, the doctor should check up whether all points have been given and conclude interrogation, if necessary with specific questions directed to elicit points which have not been obtained. For example, a patient with peptic ulcer for over ten years may forget to recall an episode of melena which occurred three years ago, and unless a leading question is asked, this information may not be forthcoming. So, also an elderly patient complaining of irregular bowel habits may not bring out the fact that he is consuming laxatives intermittently, unless specifically asked. As the patient narrates the history, the doctor should record relevant facts in a sequential manner. This art has to be learnt by constant practice by the medical student.

The history consists of the following parts:

1. Presenting complaints
2. Evolution of the disease including treatment obtained
3. Past illnesses
4. Family history
5. Social history
6. General information on diet, exercise, sleep, hobbies, occupation, recent travel and place of residence, addictions, etc.

Presenting Complaints

These are the complaints for which the patient approaches the doctor at that time and these are the ones that should receive maximum attention then. For example, a patient with chronic peptic ulcer may be coming for the presenting complaint of hematemesis; or a diabetic who is on treatment for twenty years may approach the doctor for an acute infection of the foot following shoe bite. List the presenting complaints in the order of their priority to the patient and their duration.

Evolution of the Disease

Once the presenting complaint is recorded, the next step is to elicit the evolution of the disease.

Onset

This denotes the beginning of the disorder. It may be abrupt as occurring in a myocardial infarction or hematemesis, or insidious *(meaning* pro-gressing secretly or subtly) as the vague illness occurring in cirrhosis of the liver. In many cases, acute onset of any major disaster like myocardial infarction, hematemesis, paralysis, or injury is remembered accurately by the patient. Even after years he will be able to recall the date and even the time of onset of the symptom. *Diseases in which the onset is abrupt, the course is associated with severe symptoms, and the termination is also abrupt are called acute illnesses, e.g. pneumonia, acute appendicitis, cholera and head injury. Diseases which have insidious onset, slow and protracted course with or without remissions and exacerbations and slow imperceptible termination are called chronic illnesses, e.g. chronic bronchitis with emphysema, cirrhosis liver and malnutrition*. In general, acute illnesses tend to run short courses, often ranging from days to weeks and in the majority of cases end either in cure or death. Some

may go on to chronicity, e.g. acute hepatitis C going on to chronic hepatitis, cirrhosis and even carcinoma. Treatment of these disorders produces dramatic results. On the other hand, chronic illnesses run for several months or years and in the vast majority cure is not possible. In their natural course they may get remissions and exacerbations or may proceed relentlessly to death either directly caused by the disease or one of its complications. In them, treatment seldom achieves complete recovery. Despite this, proper management helps to relieve symptoms and prevent deterioration.

Details of the evolution of the disease should be elicited carefully. The history should include the progress of symptoms as they developed, appearance of new symptoms, response to treatment, spontaneous remissions and exacerbations and other related phenomena. Details of treatment (drugs and their dosage) should be obtained as accurately as possible. Investigations including biopsy and surgical procedures should be recorded.

Complications may develop during the course of many diseases. *Complication may be defined as the development of a fresh symptom in a proportion of those suffering from a particular disease, and which deteriorates the clinical state of the patient further.*

Examples

1. During the course of typhoid fever, intestinal hemorrhage or perforation may develop.
2. During the course of myocardial infarction embolic complication may result in the development of hemiplegia.
3. During the course of poliomyelitis, paralysis may develop.

Occurrence of a complication may necessitate urgent medical intervention to prevent deterioration and death.

Past Illnesses

Record the history of past illnesses as far as the patient can remember. History of past illness gives clue to the nature of the present disease in many cases.

Examples

1. Hepatitis B infection may go on to cirrhosis liver months or years later.
2. Mumps developing in adolescence or early adulthood may be the cause of testicular atrophy and azoospermia detected later in life.
3. Reactivation of tuberculosis occurring in early life and which has been incompletely treated may be the cause of meningitis occurring in later life.

The student should bear in mind that even diseases that occurred several decades earlier may be relevant for the diagnosis of the present illness. *Three patterns may be observed.*

In the first group the presenting complaint may be a late complication of the past illness after a variable symptom-free period in between the original illness and the present one.

Examples

1. Rheumatic fever occurring in childhood leads to valvular heart disease in adolescence and adulthood.
2. Acute poststreptococcal glomerulonephritis may manifest as renal disease in late life.
3. Syphilis may manifest as primary chancre in early adulthood and go on to the secondary or tertiary stages later.

In the second group the patient may never be free of symptoms of the original disease and the presenting complaint may be one of its complications. Diabetes mellitus, systemic hypertension, and chronic bronchitis with emphysema fall in this group.

The third group is one in which an illness had occurred and subsided completely. It leads to indirect complications which may present later, e.g. osteoarthritis developing in a limb shortened by a malunited fracture.

Though in general the past history helps to correlate with present illness in many cases, in several others the two may have no relationship. Nonrecognition of this fact may lead to pitfalls in diagnosis.

Drug History

Detailed history of drug intake should be obtained in all cases. In India drugs are available freely from several sources. Unrestricted prescribing and self-administration of drugs are very common. Moreover, the same patient may follow different systems of medicine for the same or different

ailments. Drugs alter the pattern of disease, and mask the symptoms and signs, e.g. antihypertensive drugs lower the blood pressure and bronchodilator drugs relieve asthma.

Drugs may lead to complications as their side effects, e.g. corticosteroids precipitate diabetes mellitus, analgesics such as phenacetin lead to renal damage and chloroquine may provoke convulsions.

All available information about drugs should be recorded, however trivial they may appear to be. Untoward drug reactions and family history of untoward drug reactions should caution the doctor against their use in future, e.g. penicillin anaphylaxis.

Family History

Several diseases run in families. This may be caused either by genetic predisposition or similar environmental factors. Family history should be traced back from the patient *(propositus)* to as many generations as the patient can clearly remember.

Genetically Transmitted Diseases

Diseases may be transmitted from parent to offspring genetically in different patterns such as *autosomal recessive, autosomal dominant, sex-linked recessive and sex-linked dominant*. Autosomal defects are genetic defects carried on the somatic chromosomes, sex-linked defects are carried by genes present in the sex chromosomes—more frequently the X chromosomes. Autosomal disorders manifest in both sexes. Dominant genes give rise to manifestation of the disease in the offspring even if only one parent is affected and only one of the alleles in the genetic locus is abnormal. The affected subjects transmit the disease to their offsprings. Unaffected individuals are free of the disease and do not transmit it further.

Autosomal recessive diseases manifest clinically only when the patient gets the abnormal gene in homozygous form, i.e. both the alleles in the genetic locus are abnormal and both the parents carry the abnormal gene. Since both the genes are abnormal the disease occurs in a more severe form. Children of apparently normal parents may be affected.

The disease may skip generations, i.e. among the family members a particular generation may be apparently unaffected, but then next generation may manifest the disease.

Autosomal dominant inheritance: Examples of autosomal dominant disorders—achondroplasia, Marfan's syndrome, Huntington's chorea, hereditary spherocytosis, facioscapulohumeral muscular dystrophy, dystrophia myotonica, neurofibromatosis, autosomal dominant polycystic disease of the kidney, von Willebrand's disease, porphyria, Gilbert's syndrome and several others.

The affected members are from different generations. The sexes are affected equally. Fifty percent of the children of the affected parents suffer. Often one of the parents and children show the affection. Occasionally the parents and grandparents may be normal. In such cases the abnormality in the offspring may be attributable to a mutation.

Sometimes the parents may be apparently normal but the grandparent may be affected. In this situation the parent on the affected line, though possessing the abnormal gene may not be expressing the abnormality, the gene being non-penetrant.

Autosomal recessive inheritance: For example: Friedreich's ataxia, cystic fibrosis, limb girdle muscular dystrophy, Wilson's disease, albinism, ataxia telangiectasia, glycogen storage disease and others.

All the affected individuals are in the same generation. The sexes are affected equally. In any family, 25% of the children are affected. There is often consanguinity among the parents.

Sex chromosome linked disorders: Sex-linked recessive diseases are most often carried on the X chromosome and so such diseases manifest commonly in the male who has only one X chromosome derived from the mother. Mother acts as the carrier of the gene transmitting it to the male children. Female children carry the gene and they transmit the disease to successive generations without manifesting the disease except, under rare situations. The normal X chromosome derived from the father compensates and prevents disease manifestation. Male children of sisters suffer from the disease.

X-linked recessive inheritance, e.g. hemophilia, Christmas disease, G6 PD deficiency nephrogenic diabetes insipidus, Duchenne muscular dystrophy and others.

The disease affects successive generations. For a carrier female the chance of the disease developing in the sons is 50% and the chance of the daughters acting as carriers is also 50%.

X-linked dominant inheritance (e.g. hypophosphatemic type of vitamin D resistant rickets).

Since the females contain X-chromosome from both parents, they are sure to contain at least one of the affected gene, and therefore, almost all the female children are affected. They manifest the disease twice as frequently as the males, e.g. hypophosphatemic vitamin D-resistant rickets.

Y-linked Inheritance: Only males are affected. All the sons of an affected male acquire the disease whereas the daughters do not, e.g. hairy ears, webbed toes.

Mosaicism: This term refers to the presence of different chromosomal patterns in the cells of the same individual. Deletion of one of the sex chromosome or presence of an extra sex chromosome is the commonest abnormality in this group.

Chromosomal disorders: These are disorders in which cytogenetic studies reveal abnormalities of chromosome numbers and/or other features. In general, autosomal abnormalities present with the following features:

1. Mental retardation
2. Retardation of physical growth
3. Congenital malformation
4. Dysmorphic features.

For example: In Down's syndrome 3 copies of chromosome 21 are present. Other autosomal chromosome abnormalities such as trisomy may affect chromosomes 18,13 and 8. Deletion of part of chromosomes 4, 5, and 13 may occur in other conditions.

Sex chromosomal disorders: These constitute more than 50% of the congenital chromosome disorders. Deletion of an X chromosome gives rest to Turner's syndrome—usually in females, only rarely in males.

In males, presence of extra "X" chromosome give rise to Klinefelter's syndrome.

Presence of an extra Y chromosome (XYY) in males confer aggressive and criminal behavior, mental subnormality and morphological abnormalities.

After taking an accurate family history, a family tree may be constructed and this will help to identify the pattern of inheritance in most cases (Figs 1.1 to 1.4).

Environmental Factors

Many diseases occur more frequently in family members due to the same environmental factor. Typical examples include nutritional disorders, parasitic infections and contagious diseases. Rheumatic fever, tuberculosis, leprosy and post-streptococcal glomerulonephritis may affect several children in the same house. Diseases like

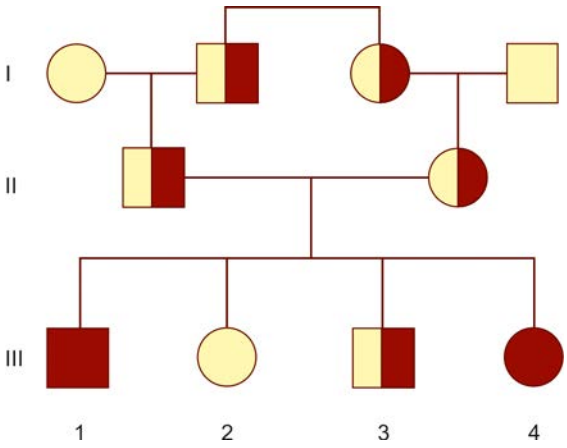


Fig. 1.1: Pedigree of a disorder with autosomal recessive inheritance (horizontal transmission). Roman numericals I-III indicate generations. The numbers 1-4 indicate siblings. Blacked out symbol means an affected individual. Those with one-half blackened indicate carriers. Circle represents female. Square represents male

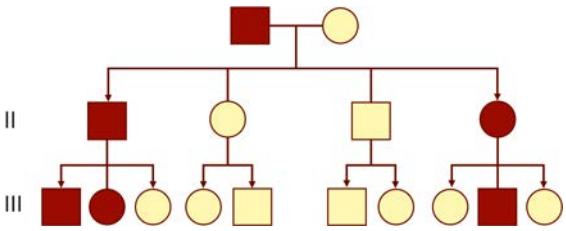


Fig. 1.2: Pedigree of a disorder with autosomal dominant inheritance (vertical transmission). Unaffected persons do not pass on the trait to their offsprings

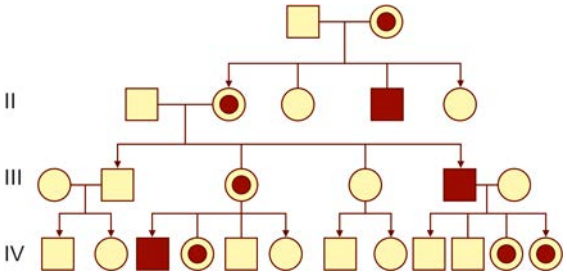


Fig. 1.3: Pedigree of a disorder with X-linked recessive inheritance (oblique transmission). Circles with dots in the center represent carrier females

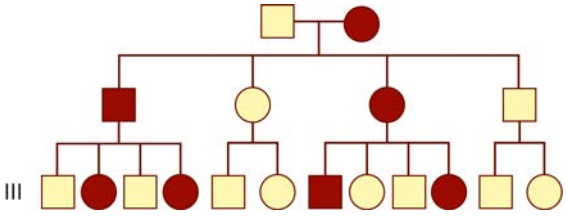


Fig. 1.4: Pedigree of a disorder with X-linked dominant inheritance. Double the number of females than males is affected

tuberculosis and leprosy which have long incubation periods and in which the organism can remain dormant may appear in the family members after a gap of several years. For example, a teenager in the house may develop acute pulmonary or lymph node tuberculosis even several years after one of the grand parents has been treated for the disease or has succumbed to it.

Personal History

This pertains to the personal habits of the individual such *as diet, work, sleep, hobbies and recreation, physical exercise, recent travel, addictions and social relationships.*

Diet plays the major role in malnutrition and transmission of several diseases. For example protein malnutrition is more common in communities where the total diet intake is low with particular reference to proteins. Vegans (those who take only food of plant origin without even dairy products) may develop deficiency of vitamin B_{12}.

Diseases may be transmitted by dietary articles. The beef tapeworm *(Taenia saginata)* is acquired by consuming infected beef. Chronic or acute toxic disorders may develop due to consumption of harmful food materials. Lathyrism and argemone oil poisoning found in many parts of India develop as a result of chronic poisoning by toxins found in *Lathyrus sativa (Khesari dal)* or argemone seeds which may be contaminating mustard seeds. Food poisoning often occurs in small or large outbreaks among persons who share the same food.

Diet rich in saturated fatty acids such as animal fats, dairy products and some of the vegetable oils such as coconut oil and palm oil tend to increase plasma low density cholesterol and this may act as one of the factors leading to atherosclerosis and coronary artery disease. On the other hand, several fish oils which contain polyunsaturated fatty acids tend to lower low density cholesterol and this may act as a protective factor against atherosclerosis. While taking dietary history, attention should be paid to the type of food, total quantity taken, timing of the diet and any particular restrictions followed by the patient, e.g. diabetic diet, salt restriction, avoidance of milk or wheat.

Many patients may have hypersensitivity (allergy) to articles of food, drugs and several other substances such as cosmetics, soaps, house dust and the like. In some cases this may be the reason for the illness. For instance, asthma may be precipitated and perpetuated by allergy to house dust, or pollen from flowers. Consumption of chocolates may be the factor leading to the development of allergic purpura. Gingivitis and lymphadenopathy may be the adverse response caused by dilantin sodium taken by epileptic patients.

Work, Leisure and Hobbies

Detailed enquiry about the work, leisure and hobbies practised by the patient often helps to arrive at the diagnosis. Dislike for the work or boredom during work is a common cause for anxiety, depression, feeling of fatigue, irritability and insomnia. Anxiety and maladaptation to work may predispose to the development of diseases such as hypertension, diabetes and coronary artery disease. Full involvement in work and its enjoyment are prime requisites for healthy mind and body. Enjoyable working conditions and a spiritual attitude towards work instills a positive attitude in life and improves its quality. Details of occupation and exposure to harmful agents should be elicited. Many occupations are associated with health hazards.

Leisure activities are essential for proper wellbeing. Each individual adopts leisure activities and hobbies depending on his mental make up and circumstances. These reduce mental tension, relieve fatigue, make life more pleasurable and establish better family and social relationships. Hobbies may expose the person to infective agents, e.g. contact with parrots may lead to psittacosis.

Physical Exercise

Details of physical exercise have to be enquired into. Physical exercise helps to keep the bodily functions intact, maintains mobility and alertness of the locomotor system, and delays the onset of ischemic and degenerative changes in the cardiovascular and nervous systems. It also promotes well being. Individuals vary in the pattern of exercise. Daily work schedule can be classified as 'sedentary' (those that do not involve any physical activity or exertion) and 'active' in which physical activity of varying degrees is built in. Many do not undertake any exercise at all. Work or physical activity done along with routine duties should not be equated with "exercise" done as a leisure activity. The latter is the one more conducive to better health. Sedentary occupations which involve very little of physical activity are associated with higher incidence of obesity, ischemic heart disease and diabetes mellitus. The definite beneficial influence of regular physical exercise in preventing the onset of degenerative diseases such as obesity, atherosclerosis and metabolic disorders such as diabetes mellitus has been proved beyond doubt. At least four or five sessions of vigorous games or walking 3 to 4 km in 30 to 45 minutes constitutes adequate health-promoting exercise, if undertaken every week.

Menstrual History

In women, the onset of menstruation (menarche) and its details, pregnancy, abortions, contraceptive practices and menopause should be recorded. Several diseases occur in women during the reproductive period. Menopause is associated with medical problems such as hot flushes. Postmenopausal women are prone to develop osteoporosis. Whereas ischemic heart disease is rare in premenopausal women, its incidence shoots up after menopause.

Family Relationships

Healthy family life is a prerequisite to proper mental and physical development. Details of sexual activity should be enquired into. Healthy sex habits are essential for marital happiness, proper conjugal relationship and the development of family ties. Details of sexual activity, failure in sexual performance, and anxiety and misconceptions about sex should be elicited.

Premarital and extramarital sexual relationships and exposure to high-risk groups such as prostitutes, homosexual partners and drug addicts should be enquired into. Sexually transmitted diseases such as syphilis, gonorrhea, nongonococcal urethritis, AIDS (acquired immune deficiency syndrome) and several others are usually acquired by extramarital sexual exposures. Occurrence of sexually transmitted disease in the spouse may give clue to the nature of disease in the partner.

Several diseases such as AIDS, viral hepatitis, syphilis and malaria spread through blood transfusion. In India, a small proportion of patients acquire these diseases through improperly administered blood and blood products.

Belief in any religious faith or ideology is an important factor which determines the psychological make-up of humans. Irrespective of the religious faith, those who profess religious tenets show more balanced mental attitude towards disease and their morale to overcome the disease is better. They are more reliable in taking therapy.

Socioeconomic Factors

Several diseases are more prevalent among different ethnic groups. This is due to the wider prevalence of the genetic defects in the community as a result of intermarriage. Typical examples are the higher prevalence of sickle cell disease in tribal populations in the different parts of India. Other hereditary diseases which show this feature are thalassemias, glucose-6-phosphate dehydrogenase (G6PD) deficiency, Wilson's disease and the like, poverty, squalor and illiteracy often go hand in hand. These are associated with malnutrition, increased incidence of infectious diseases, nonacceptance of family welfare advice and considerably low health standards. Diseases of children such as kwashiorkor, intestinal helminths, scabies, rheumatic

fever, acute post-streptococcal glomerulonephritis, infective diarrheas, respiratory infections and poliomyelitis are much more common in them. The coverage by childhood immunization programs is also less among them. As the socioeconomic condition and literacy among mothers improve, there is a dramatic fall in these diseases and health standards rapidly improve.

Affluence on the other hand, brings in its turn a new set of health problems. Obesity, diabetes, systemic hypertension and ischemic heart disease are more prevalent among this group. This increase is partly due to overeating, reduction in physical activity, heavy indulgence in tobacco smoking and alcohol and increase in mental tension. In India, overweight and obesity are seen in the lower socio-economic groups as well, though in much smaller proportions.

In all countries the poor also suffer from non-availability of health care services due to economic considerations as well as lack of awareness As a result, they have higher mortality and morbidity rates in comparison to the well-to-do.

Details of Place of Residence and Recent Travel

Several diseases are endemic in many geograp-hical areas. Malaria is prevalent in almost all states of India. In Kerala, though there are a few pockets of endemic malaria, the majority of cases are imported from other states of India or from other countries in Arabian Gulf or Africa where malaria is endemic. *Plasmodium falciparum* (malignant tertian) malaria is more prevalent in the north eastern states. More than 50% are resistant to chloroquine and other antimalarial drugs. Filariasis *(Wuchereria bancrofti* and *Brugia malayi)* is prevalent in many parts of India, Bancroftian filariasis is much more widespread, whereas *B. malayi* is confined to limited areas, particularly in the coastal districts of Kerala. Loiasis and onchocerciasis are prevalent in Africa. Hydatid disease is more prevalent in Tamilnadu. Cysticercosis is prevalent in many states in India and is a frequent cause of adult onset seizures, Guinea worm *(Dracunculus medinensis)* is prevalent in Andhra Pradesh, Rajasthan and Punjab. The incidence of this infestation has been brought down considerably through national eradication program. Endemic fluorosis is widespread in many parts of Punjab, Uttar Pradesh, Andhra Pradesh and Karnataka. Calcific pancreatitis and endomyocardial fibrosis are probably more prevalent in Kerala.

Visit to any place in the recent past and details of the diseases prevalent in the region should be carefully asked for.

Addictions

Addictions (syn): Habituation, substance abuse.

Habituation to substances like tobacco, alcohol, opium, cannabis, cocaine and many others has been a feature of mankind from time immemorial. One feature which is common for all these substances is that they produce alterations in mood, mask anxiety and tension and promote social relationships. Therefore, they are all widely used in many societies. Their regular use leads to tolerance and addiction. A common factor for all of them is that they act on the central nervous system. In small doses they may stimulate certain neurological functions, but in larger doses they are depressants. Addiction, habituation and dependence are terms used to denote the condition when an individual becomes dependent on the drug for maintaining ordinary state of mental and physical functions and withdrawal of which leads to craving and withdrawal symptoms. In modern societies drug dependence is a great social evil. Drug trafficking and smuggling of drugs internationally are crimes which have reached great proportions.

Drug addiction is more frequent in children of families where the elders use drugs. Initially started as a social habit, the narcotic soon overpowers the victim and causes dependence and its further problems.

Tobacco is used in several forms—for chewing, as a snuff or for smoking *in bidees (biris)*, cigarettes, cigars, pipes, and *hooka*. Smoking is the most common mode of use. Nicotine content of tobacco is responsible for causing addiction. One cigarette contains 1.2 to 1.4 mg of nicotine and beedi contains a third of this.

Tabacco smoking leads to cumulative morbidity in several systems in the body. Some of the common diseases attributable directly or indirectly to tobacco smoking are:

Respiratory system: Chronic bronchitis with emphysema, bronchogenic carcinoma.

Cardiovascular system: Ischemic heart disease, hypertension, atheroma, thromboangiitis obliterans.

Alimentary system: Acid peptic disease.

Passive smoking is the term used to denote the inhalation of tobacco smoke by nonsmokers from an environment which has been contaminated by a smoker. Passive smoking is also attended with harm though to a lesser extent. Passive smoking in closed environments such as bed rooms or transport vehicles leads to considerable morbidity in those affected, particularly in women and children.

Though smoking is more widespread among males, the proportion of smokers among women is steadily increasing. Smoking during pregnancy can lead to ill-effects in the fetus as well. In many countries either by legislation or by voluntary consent, smoking in public places, aircraft and ceremonial occasions has been banned. Though in the developed countries the sale of cigarettes has come down, this trend has not set in robustly in India. The Government of India insists on a statutory provision to indicate the danger of cigarette smoking on the packet. But such a legislation has not come in the case of *bidees,* which is a product of cottage industry providing occupation for many workers. The practice of smoking beedies with the lighted end kept inside the mouth, as is seen in Andhra Pradesh, and Karnataka is a common cause for palatal cancer. Several other cancers such as oral cancer, esophageal cancer and cancers in remote systems are causally related to tobacco smoke.

Another common form of tobacco use is chewing *"pan"* which consists of betel leaf, lime, arecanut and tobacco. Nicotine is absorbed from the oral mucosa. The amount of tobacco used and the frequency of chewing vary. Many people keep the material in the mouth for long periods. Keeping the material in the mouth for long periods predisposes to the development of oral cancers which are among the most common cancers in males seen in many parts of India.

Alcohol is consumed in several forms: Several preparations are available commercially. The common forms are toddy (alcohol content 5%) beer (5%), wines (10%), arrack (illicitly made (40-60 %), gin, whisky and brandy (45-60%). One standard drink contains 12 g alcohol. 180 mL wine, 360 mL beer or toddy or 45 mL of the spirits give 18- 20 mL of alcohol. When taken in excess it leads to several diseases. Alcohol supplies calories, but it is not a proximate principle of food. In the early stages of alcohol consumption, the person puts on weight, but as the quantity of alcohol increases progressively, consumption of food articles falls and it leads to various forms of malnutrition. The liver is the most common organ to be affected. *Alcoholic hepatitis*, fatty change in the liver and *cirrhosis* are the common sequelae of alcoholism. Other diseases attributable to alcohol include *peripheral neuropathy, Wernicke's encephalopathy, Korsakoff's psychosis, cardiomyopathy and immune suppression.*

Several other substances are employed by the youth as "stimulants" which lead to *drug dependence*. These include *cannabis, ganja, bhang, lysergic acid derivatives, cocaine, sedative and hyponotic drugs, dexidrine* and others. The proportion of drug addicts among school and college students is on the rise. Use of injectible drugs in small groups sharing the same needle and syringe is a common practice in many countries. Sharing of needles is a cause for spread of diseases such as AIDS and hepatitis and right sided endocarditis in them. Use of cocaine predisposes to ischemia and other heart disease.

In addition to adverse physical effects on the individual, alcoholism and addiction to cannabis, and other psychedelic drugs result in degeneration of personality and mental faculties. Economic problems and disruption of family relationships follow. The subject of drug addiction is a major speciality by itself and the student may refer to texts on this subject for further details.

While enquiring about addiction, details of the substances consumed, their dose and frequency, duration of use and their possible effect on health should be ascertained.

After completing interrogation the details should be recorded sequentially and in more than 50% of cases the pattern of disease will give the most important clue to diagnosis. *Even today history remains the most effective procedure* to *enlist the*

patient's confidence and satisfaction in the patient-doctor relationship. This skill should be developed by the young doctor from the early part of his career.

The Diagnostic Process

The history leads the doctor to very near the possible groups of diseases which the patient may be suffering from. From there on he has to follow a well-defined and time tested procedure to arrive at the most likely diagnosis. These include physical examination, investigations and follow up. All these are described in subsequent chapters. Investigations have become integral part of the diagnostic process. They are expensive, many of them are invasive (capable of doing harm) and some of them are not absolutely conclusive too. Choice of investigation and its performance have to be guided by established norms. The doctor has to be aware of the evidence base about these investigations in order to be efficient and patient-friendly.

EVIDENCE-BASED MEDICINE AND DIAGNOSTIC TEST EVALUATION

Evidence-based medicine (EBM) is a combination of systematic reviews of medical literature, mega randomized trials and meta-analysis of randomized trials. Sackett has defined EBM as "the conscientious, explicit and judicious use of current best in making decisions about the care of individual patients. It requires the integration of clinical expertise, external evidence, and patient's values and expectations." The types of evidence may be classified as:

1. Evidence obtained from meta analysis of randomized controlled trials.
2. Evidence obtained from at least one large randomized control trials.
3. Evidence obtained from at least one large well designed controlled study without randomization.
4. Evidence obtained from well designed quasi experimental study.
5. Evidence obtained from well designed non experimental descriptive studies such as comparative studies, correlation studies, and case control studies.
6. Evidence obtained from expert committee reports or opinion and/or clinical experience of respected authorities.

Most would only accept (1) and (2) in making any emphatic recommendation on management. The other levels of evidence would indicate the need for randomized controlled studies but may, on the short-term be used to guide management even before completion and publication of results. Clearly these criteria for an evidence base do not take into account clinical judgment and experience; quality factors; attitudes of patients and their relatives; and demands related to individual clinical consultations. They are also encumbered by publication bias.

Thus, in designing clinical guidelines, the priority should be to access the evidence base that is available and to ensure that it has been correctly interpreted so that when followed, can lead to improvements in health. It is also important to establish whether the outcome would be the same when employed in different clinical circumstances.

Diagnostic Test in Relation to the Disease Process

The use of diagnostic tests is essential in understanding the disease process. Much effort is devoted to the understanding of disease processes at the individual, organ, cellular and genetic levels, without proper consideration to the interplay between the individual and his social environment. At the population level the use of diagnostic tests is made more complicated by population effects such as prevalence of the pathogen, expression and impact of the disease on the population and potential for pathogen spread among others, multifactorial causes of disease and the impact of predisposing factors.

Figure 1.5 neatly illustrates the complex interplay of factors which result in disease at the individual and population levels. This implies that the presence of a pathogen may not, in itself, be sufficient to cause disease in the absence of other factors, a concept expressed in the statement that a pathogen is a *necessary* but not *sufficient* cause for a particular disease. Application of these concepts requires a different approach for the interpretation of diagnostic test results, particularly where they are applied for a decision-making process.

The Investigative Process

Present day diagnostic process depends on investigations in addition to forming clinical

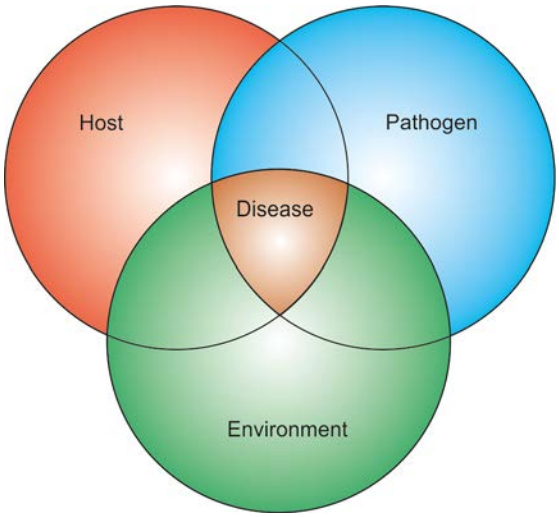


Fig. 1.5: Figure giving the familiar "epidemiological triad" concept

impressions. Several different investigations are available at present. Many of them are reasonably priced, noninvasive and clear-cut in their results, e.g. culture and sensitivity of bacteria. Many others are expensive, not clear-cut in their results and may even be invasive, e.g. biopsies, serological tests. Therefore, it is essential that the doctor is aware of basic facts in present day knowledge before undertaking investigations in a cost-effective and maximally useful manner. For this purpose the information from evidence based medicine (EBM) assumes great importance. It is also absolutely essential that the doctor is aware of all the implications before ordering tests so as to be quite clear of the legal liabilities that may also arise. Medical decision analysis involves quantitative approach to medical decision making. Mystery of clinical reasoning involves cognitive process used to discard or confirm a diagnostic state. One would like to find answers to the following questions:

1. How may I be thorough, yet efficient when considering the possible causes of my patient's problems?
2. How do I characterize the information I have gathered during medical interview and physical examination?
3. How should I interpret new diagnostic information? How do I select the appropriate diagnostic test?
4. How do I choose among several risky treatments?

A diagnosis is a statement of an individual's state of "normality" and represents an interpretation of one or several observations that form the basis for a decision for further action. The decision is based on a number of factors including factual knowledge, experience and intuition as well as clinical diagnostic tests and it is the correct use of all of these which increases the probability of correct diagnosis (Fig. 1.6). This definition clearly identifies the uncertainty associated with diagnosis and the outcome of a given course of action taken as a result.

Selection of a Diagnostic Test

The selection of an appropriate diagnostic test depends upon the intended use of the results. If the intention is to rule out a disease, reliable negative results are required for which a test with high sensitivity (only a few false negatives) is used. If it is desired to confirm a diagnosis or find evidence of disease (i.e. to "rule in" the disease) we require a test with reliable positive results (i.e. high specificity). As a general rule of thumb, a test with at least 95% sensitivity and 75% specificity should be used to rule out a disease and one with at least 95% specificity and 75% sensitivity used to rule in a disease.

Selection of diagnostic test is important because it rarely reveals patients' true state with certainty. Order of a diagnostic test should be restricted to those tests where results could alter management decisions. But physicians often start treatment despite uncertainty. The level of certainty at which

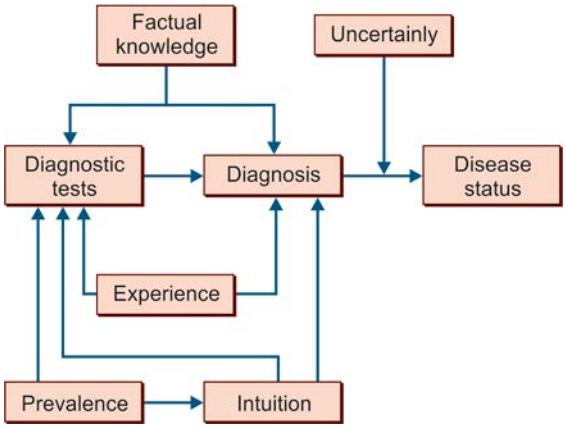


Fig. 1.6: Factors influencing diagnosis probability of correct diagnosis

Table 1.1: Selection of diagnostic tests

Test characteristics	*Definition*
Sensitivity	Proportion of people with the disease in whom test is positive (i.e. proportion of true positives).
Specificity	Proportion of people without the disease in whom test is negative (i.e. proportion of true negatives)
Positive predictive value	The probability (or likelihood) that a person that returns a positive test result actually has the disease in question.
Negative predictive value	The probability (or likelihood) that a person that returns a negative test result actually does not have the disease in question.
Accuracy	The accuracy of a test refers to the level of agreement between the test result and the "true" clinical state.
Precision	Represents the degree of fluctuation of a series of measurements around the central measurement.
True prevalence	Proportion of persons in the population which really do have the disease in question regardless of their test result. From a test result point of view, it includes the "true" positives and the "false" negatives as well.

a clinician is willing to start treatment influences selection of diagnostic test. This level of certainly is known as treatmental threshold probability. At this level one has to document risks and benefits of treatment. Also assess patient's feelings about the risks and benefits of treatment in terms of utility (Table 1.1).

Diagnostic tests are more or less objective methods which reduce the uncertainty factor in diagnosis. Diagnostic tests are often interpreted using a dichotomous outcome (normal/abnormal, diseased/healthy, treat/don't treat) which poses less difficulty when the test itself is a dichotomous variable (presence or absence of a pathogen) but can cause considerable difficulty in interpretation when it is continuous (e.g. serum antibody levels or cell counts). In such cases, the selection of an appropriate cut-off point to separate 'positive' and 'negative' results introduces a level of uncertainty. In most diagnostic tests false positives and false negatives occur. Consequently, any diagnostic test which does not directly identify the presence of the infection can only produce an estimate of the apparent prevalence of a disease (i.e. the proportion of individuals giving a positive test result) and does not equate to the presence of infection. Estimates of true prevalence, however, can be made taking into account test sensitivity and specificity where these are known.

Table 1.2: True status of disease

Test result	*Disease status*		*Total*
	Diseased	*Not diseased*	
Positive	(a) True positive	(b) False positive	a + b
Negative	(c) False negative	(d) True negative	c + d
Total	a + c	b + d	a + b + c + d

Sensitivity and specificity are indicators of the validity of diagnostic tests. When a cut-off point is used, sensitivity and specificity show an inverse relationship—as sensitivity increases, specificity decreases and vice versa. Estimation of the sensitivity and specificity requires testing of persons for which the disease status is known. This requires the use of an appropriate unequivocal diagnostic method as a "gold standard". For example, the histological demonstration of the disease may be used as estimation of true status (the "gold standard") and to evaluate the PCR data obtained by constructing the following simple tables (Table 1.2).

In the Table 1.2, "a" represents the true positives, "d" the true negatives and "b" and "c" the false positives and false negatives respectively. The various epidemiological values can also be simply calculated as follows:

- Sensitivity = a/(a+c)
- Specificity = d/(b+d)
- Positive predictive value (PPV) = a/(a+b)
- Negative predictive value (NPV) = d/(c+d)
- Apparent prevalence = a+b/(a+b+c+d)
- True prevalence = a/(a+b+c+d).

The selection of the appropriate level of sensitivity and specificity often depends upon the particular need. When screening for a disease or pathogen (for example, testing persons to eliminate infected individuals) we require a reliable positive result with only a few false negatives and only a reasonable number of false positives (within an economically justifiable level of rejection). This would require a test with a high sensitivity and reasonable specificity. This type of test would be used in a quarantine situation, for example, to reduce the risk of disease introduction in to a community or when demonstrating absence of a disease to establish

"disease-free" zones. On the other hand, if we need as few false positives as possible (e.g. to confirm a tentative diagnosis) a test with a high specificity and reasonable sensitivity is used. It is, however, important to note that the consequence of any diagnostic test with imperfect specificity (less than 100%) is that if a large number of tests are made on a single uninfected individual, there is a significant chance of finding a positive result.

Predictive Values

For a diagnostic decision, it is also useful to make some estimate of the predictive value of a diagnostic test. The predictive value quantifies the probability that a positive test result for a particular person or sample correctly identifies the presence of infection and a negative test result correctly identifies the absence of infection. This requires knowledge of not only the sensitivity and specificity of the test but the prevalence of the condition. The effect of prevalence on predictive values is considerable. As prevalence increases, positive predictive value (PPV) increases and negative predictive value (NPV) decreases.

Formulae for calculating predictive values are based on Bayes' theorem of conditional probability. Predictive values are functions of prevalence and the test characteristics of sensitivity and specificity. As prevalence declines so does positive predictive value. The converse is true for negative predictive value.

If the sensitivity and specificity of a diagnostic test are known for a particular target population, then predictive value graphs can be drawn for the range of all possible pretest probabilities of disease from 0 to 1 (100%).

Interpretation of New Diagnostic Test

A diagnostic test may not always reveal the patient's true state. Hence, one has to estimate how much the new information has changed the uncertainty. Bayes' theorem helps to estimate the change in probability. Estimates of probability of a disease before new information is available is known as *prior probability*. Estimate that results after new test information is available and is known as *posterior probability*.

SECTION

2

General Examination and Imagiology

CHAPTER

2 General Examination

PK Sasidharan

General examination, Fever, Fever of unknown origin, Level of consciousness, Anthropometry, Congenital abnormalities, Weight and nutrition, Pallor, Jaundice, Cyanosis, Clubbing of fingers, Nail changes, Skin, Hair distribution, Edema, Lymph nodes

INTRODUCTION

Patient evaluation starts the moment we watch the patient or establish eye contact with the patient. Be alert, use all faculties of sense (vision, hearing, smell, touch) to pick up important clues to the diagnosis, the process of history taking continues till we complete the clinical examination. The clinician should be observing the way he greets, sits, walks, talks; or in short anything that the patient does in front of us is subjected to evaluation by an astute clinician. Finally some patients and relatives might get the feeling that the doctor made the diagnosis by just palpating pulse and some intelligent persons even conclude that the doctor is able to smell the diagnosis !!!. That is good clinical skill and is not intuition. Like history taking the general examination also continues *throughout* the period of evaluation and finishes only at the end of the interaction with the patient. In real life practice it is desirable that the physical examination should start with the area mainly affected, only to give confidence to the patient and to reinforce the reassurance. Remember that the eyes won't see what the mind does not know, and be aware of the abnormalities possible in each area. The order in which physical examination is done is decided by the convenience of the patient *primarily* and sometimes decided by the convenience of the doctor.

Before proceeding to physical examination, remember to obtain consent from the patient. In the case of children and persons who are not able to give consent, permission should be obtained from the next of kin or legal guardian. In medicolegal cases, physical examination may have to be done under direction from the appropriate authority. Irrespective of the presenting complaint, it is necessary to perform general examination and then to proceed to systemic examination. Gentleness and concern for the patient are essential to get the best results.

GENERAL EXAMINATION

Perform general examination with the following objectives:

1. To get an overall impression about the general state of health.
2. To obtain cooperation for further detailed examination.
3. To decide on the immediate intervention required, for example, a patient in shock requires immediate resuscitatory measures to save life, rather than a detailed physical examination which will lead to delay in instituting life support (Some of the other common situations where the physician has to take immediate resuscitatory measures based on history and general examination are sudden collapse, respiratory obstruction, trauma, drowning, poisoning, convulsions, snake bite, anaphylactic reactions, bleeding, hyperpyrexia, coma and the like).

The general examination may draw attention to the system that is maximally deranged so that the physician can start systematic examination with that system first and proceed to the rest, usually done is a head to foot manner.

The following signs should be looked for in the general examination:

1. Behavior, attitude and posture
2. Build and nutrition
 a. Height
 b. Weight
 c. Body Mass Index (BMI)
 d. Anthropometric features
 e. Congenital abnormalities
3. Temperature
4. Pallor
5. Jaundice
6. Cyanosis
7. Clubbing of fingers and toes, abnormalities of nails
8. Abnormalities of skin and hair
9. Edema
10. Lymphadenopathy
11. Vital signs.

Do not forget to include those features which are not usually mentioned in systemic examination but noted during a head to foot examination of the patient. For example, examination for external features of thyroid disease (hypo and hyper-thyroidism), chronic liver and kidney disease, connective tissue disease, diabetes, metabolic syndrome, etc. should be part of general examination. Careful observation, inspection and palpation are the methods used for general examination, where required, percussion and auscultation also should be used as part of general examination, e.g. during examination of swellings or peripheral pulses. One may start with vital signs, especially in a very sick patient, but it may be other way round while sitting in the OPD or while evaluating a stable patient; Vital signs include the pulse, respiratory rate, blood pressure, temperature and the level of consciousness. Always stand on the right side of the patient unless the clinician is left handed and is trained to do the examination standing on the left side.

Pulse

The radial pulse should be examined and its rate, rhythm and character noted. The right radial pulse is palpated with the tips of three fingers of the left hand, with the wrist slightly flexed and supported by the right hand to relax the muscles (Fig. 2.1). Normal pulse rate is 80 (60–100) per minute. Tachycardia (rate above 100/mt) may occur due to anxiety, exercise, fever, hyperthyroidism and tachyarrhythmias. In shock the pulse is rapid and thready, i.e. low volume and fast rate. Bradycardia (rate below 60/minute) is common in those who do hard physical labor and in trained athletes. Rates below 40/minute should raise the suspicion of heart block, especially so if there is no increase on exertion.

Respiration

Respiratory rate is counted by watching the movement of the abdomen, while the examiner pretends as if he is palpating the pulse. This is to divert the attention of the patient, from the abdomen which the examiner is observing (Fig. 2.2). Normal respiratory rate is 14–18/minute. Rise in respiratory rate occurs in conditions with increased work of breathing or due to stimulation of respiratory center. Diseases like pneumonia, pleural effusion, pulmonary



Fig. 2.1: Palpation of pulse



Fig. 2.2: Counting respiratory rate

edema or bronchial asthma increase work of breathing. Stimulation of respiratory center can be due to hypoxia or low pH hence, can be seen in pulmonary embolism, and metabolic acidosis. Anxiety also stimulates the respiratory center. In shock, patients have severe tachypnea with signs of respiratory distress due to multiple mechanisms. Respiratory rate is considerably diminished in narcotic poisoning, raised intracranial tension and in deep coma.

Blood Pressure

The patient is seated comfortably or lying down, blood pressure (BP) cuff of adequate size is tied snugly not very loose or very tight, permitting introduction of one finger. The center of the cuff should be lying over the brachial artery, tie the cuff in such a way that the tubing of the cuff will not interfere with auscultation. The adequacy of the size of the cuff is assessed by ensuring that it covers three fourth the circumference of the upper arm, and two third the length of the upper arm. Tie it 2 to 3 cm above the elbow joint. The hand should be kept in a position to ensure that the cuff remains at the level of the heart. Palpating the radial pulse, the cuff is inflated as quickly as possible till the pressure in the cuff is sufficient to obliterate the pulse and further raise it to 20 to 30 mm above that level (Fig. 2.3). Keeping the stethoscope over the brachial artery at the elbow, the pressure in the cuff is released as slowly as possible,1–2 divisions at a time, till the Korotkov sounds are heard, the level at which the first sound is heard corresponds to systolic pressure. Continue the deflation of the cuff at the same rate as before, and note down the pressure at which the sounds muffle sharply or disappear and that is an estimate of diastolic pressure (Fig. 2.4).



Fig. 2.3: Palpating radial pulse and inflating the cuff

Blood pressure gives an indication of the overall cardiovascular status since it depends upon cardiac output and peripheral resistance. Fall in either, leads to drop in blood pressure. Normal blood pressure in adults is 100 to 120 mm Hg systolic and 70 to 84 mm Hg diastolic. Normal blood pressure differs at different ages and during pregnancy. Any increase in blood pressure above the expected normal (both systolic and diastolic or isolated systolic or diastolic) for the age and sex is hypertension. Hypertension is increasing in prevalence due to changing diet and lifestyle in India. Elevation of blood pressure is seen in systemic hypertension, increased intracranial tension, and several other diseases characterized by increase in hormones which raise blood pressure. In shock the blood pressure drops and reaches values below 80/40 in adults.

Temperature

Whether or not a patient is febrile is often obvious by palpation of the forehead with the dorsum of the hand (Fig. 2.5). But the exact temperature



Fig. 2.4: Auscultating brachial artery and deflating the cuff



Fig. 2.5: Palpating to detect fever



Fig. 2.6: Measuring temperature

has to be recorded in doubtful cases to document fever and to assess the height of temperature using a clinical thermometer (see measurement of temperature) (Fig. 2.6).

Recording of Temperature

Do not touch bulb of the thermometer, shake down the mercury column into the bulb, keep it under the tongue with the mouth closed for one minute before reading the temperature. Make sure that the patient has not taken hot or cold liquids or solids at least 15 minutes prior to examination, which can lead to wrong recordings. Other areas from which temperature can be recorded are the axilla and the rectum. Oral temperature ranges between 37 to 37.2°C in health. Axillary temperature is lower than oral temperature by 0.5°C and the rectal temperature may be higher by 0.5°C. Rectal temperature is closer to core temperature. Several advancements have come in the recording of temperature. These include the use of thermocouples, digital thermometers and the use of strips, which when applied over the skin, read the temperature straight away. Highly accurate recordings are essential for monitoring the patient during major surgery (extra corporeal circulation, hypothermia) and for research purposes. For ordinary purposes clinical thermometers are adequate. Humans are homeothermic (warm blooded) and therefore under widely varying environmental conditions the temperature of the central parts of the body is kept around 37°C. In premature babies and newborns the mechanisms which regulate body temperature are not fully developed. Therefore, they run the risk of hypothermia if exposed to cold environment.

FEVER (PYREXIA)

It is the abnormal elevation of temperature above 37.2°C in the morning and 37.7°C in the evening. In many cases it is associated with other features such as discomfort, burning of the eyes, chills, rigors, aches and pains and malaise. Presence of fever is a definite indication for proper evaluation, and if the cause is not obvious it necessitates review of history and physical signs, laboratory investigation and close observation. The temperature is elevated by increasing heat production and reducing heat loss. Heat production is increased by increasing the metabolic rate and rapid muscular contractions as in rigors. Heat loss by radiation is reduced by peripheral vasoconstriction. Rise of temperature may occur abruptly within hours as in pneumococcal pneumonia or influenza or it may be gradual and step-ladder type as in enteric fever and brucellosis. It is essential to record the temperature once in four hours or even more frequently to identify the pattern of fever. It is a golden rule not to wake up a sleeping patient for recording the temperature. In all patients the temperature tends to swing during different periods of the day, maximum being in the evenings and minimum during early hours of the morning.

Patterns of Fever

Continuous fever: The temperature is elevated all the time but the difference between the maximum and minimum does not exceed 1ºC, e.g. early stages of pneumonia (Fig. 2.7).

Remittent fever: The temperature is elevated throughout but the fluctuation is more than 1ºC, e.g. enteric fever.

Intermittent fever: The temperature rises and falls, touching normal in between the peaks, e.g. malaria.

Presence of chills and rigor suggests rapid rise of temperature (Fig. 2.8), as occurring in malaria,

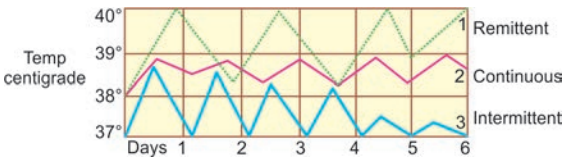


Fig. 2.7: Patterns of fever
(1) Remittent, (2) Continuous, (3) Intermittent

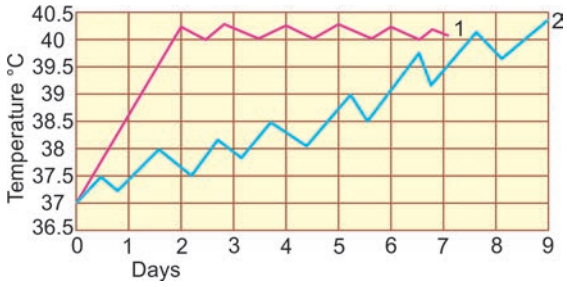


Fig. 2.8: The pattern of rise of temperature
(1) Abrupt rise (2) Step-ladder pattern

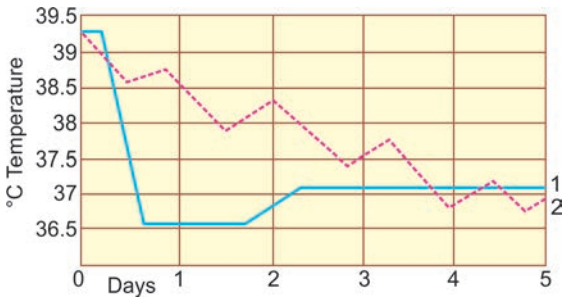


Fig. 2.9: Pattern of the fall of temperature
(1) Fall by crisis, (2) Fall by lysis

pyelonephritis, pus collection somewhere and cholangitis.

Periodicity: Many intermittent fevers show periodicity. The fever recurs at regular intervals. Typically seen in malraia, but in *P. falciparum* malaria and in mixed infections by different species of parasites, sometimes periodicity may not be observed.

Fever occurring every day is the usual phenomenon (subtertian fever/quotidian fever), e.g. typhoid, leishmaniasis, falciparum malaria. Fever occurring on alternate days is called tertian periodicity, e.g. *Plasmodium vivax* malaria . Fever occurring once in every fourth day (i.e. with intervals of 2 days in between) is called quartan fever, e.g. *Plasmodium malariae* malaria (quartan malaria).

Pel-Ebstein's fever: This is cyclic fever in which fever lasting for 3 to 10 days alternates with afebrile periods of the same duration, e.g. some cases of Hodgkin's disease.

Hyperpyrexia and Hyperthermia

Hyperpyrexia denotes high temperature, equal to or more than 41°C. It results from the setting of the hypothalamic thermostat to a higher level or loss of control of the thermoregulatory mechanism. It may be observed in severe infections, intracranial haemorrhage, heat stroke, drug induced conditions (e.g.) anticholinergics, neuroleptic malignant syndrome (NMS), malignant hyperthermia and thyrotoxic crisis. If there is uncontrolled production of body heat exceeding the ability of the body to dissipate it, hyperthermia may result. Hyperthermia is a medical emergency with high mortality and morbidity. This condition has to be anticipated and managed effectively to save life.

Patterns of fall of temperature (defervescence), see Figure 2.9.

Crisis: This refers to an abrupt fall of temperature from a high level (40°C or above) to subnormal values within a few hours, e.g. pneumococcal pneumonia. Crisis is accompanied by severe sweating (diaphoresis), often diuresis and in some cases diarrhea. The blood pressure may drop and the patient may develop signs of shock.

Lysis: The temperature falls in steps day by day to reach normal over a few days. In many cases it falls to subnormal levels, after which the fever subsides, e.g. typhoid fever.

Importance of Fevers

Fever is a very common sign indicating disease. It is a general nonspecific reaction of the body in response to several types of stimuli. It is more common during childhood. The pattern of fever gives clue to the possible underlying cause in many cases and therefore, it is essential to record the temperature regularly.

Examples

Pneumococcal pneumonia: Abrupt onset, continuous fever, fall by crisis.

Typhoid fever: Slow onset with step-ladder pattern, continuous or remittent fever, fall by lysis.

Plasmodium vivax malaria: Intermittent fever-tertian periodicity.

Administration of antipyretics at the commencement of fever alters its pattern and abolishes its diagnostic value.

General Accompaniments of Fever

The basal metabolic rate is increased. Excess catabolic activity leads to rapid loss of weight. This is aggravated by diminution in food intake which is caused by loss of appetite (anorexia) which is a common accompaniment of fevers.

The insensible fluid losses are increased. The patient tends to get dehydrated.

The heart rate increases at the rate of 18 counts per minute for every 1°C rise of temperature. This results from increased rate of the SA node. The relationship between the pulse rate and the temperature level gives diagnostic clues. Fevers in which the heart rate is not raised proportional to the temperature are called slow pulse fevers (relative bradycardia), e.g. typhoid, meningitis, influenza. Those in which the pulse rate rises out of proportion to the rise in temperature are called rapid pulse fevers, e.g. rheumatic fever, tuberculosis, pneumonia.

Respiratory rate: In general the ratio of the respiratory rate to heart rate is around 1:4. Respiratory rate increases in fevers along with the heart rate. Abnormal elevation of respiratory rate out of proportion to the heart rate occurs in respiratory diseases such as pneumonias and pleural effusion.

Rashes

These are eruptions occurring over the skin or mucous membranes and may of them are associated with fevers. They are of diagnostic importance. The rash may be macular, papular, vesicular, pustular or hemorrhagic. Fevers characterized by the occurrence of rashes over the skin are called exanthematous fevers. If the rashes occur in the mucous membranes they are called enanthems. The distribution of the rashes and the time of their appearance are characteristic.

Time of Appearance of the Rash

Skin rash occurring on the:

First day of fever	Chickenpox
Second day	Scarlet fever
Third day	Smallpox (eradicated)
Fourth day	Measles
Fifth day	Typhus
Sixth day	Typhoid (rose spots, but usually not seen in Indian patients)

Early administration of antipyretics and other drugs alter the natural history of the disease. Rashes may also be due to adverse reaction to drugs.

Patterns of Rashes

Koplik's spots are bluish gray spots occurring inside the cheeks opposite the upper second molars in measles, before the skin rashes appear. These are diagnostic.

Maculopapular rash over the butterfly area of the face is highly suggestive of systemic lupus erythematosus.

Erythema marginatum in rheumatic fever, coppery rash in secondary syphilis, hemorrhagic rash in meningococcemia.

Erythema chronicum migrans in Lyme disease are only a few of the many examples.

In addition to these, it is common to get allergic rashes caused by medications. These have to be distinguished by proper history and clinical features. Drug rashes are commonly due to hypersensitivity. Majority of them are pruritic and associated with other allergic manifestations.

Mouth

Appetite is lost in most fevers and the intake of food and fluids come down. The mouth becomes dry and coated. Presence of dried up debris over the teeth at the level of lip margins is called "sordes". The pattern of coating of the tongue may be characteristic. In typhoid fever the tongue shows central coating, the margins being free.

In many cases the tongue may show other changes:

Soreness of the tongue: Measles.

Red beefy tongue: Broad-spectrum antibiotic therapy.

White curdy membrane over the tongue easily removable: Candidiasis due to prolonged broad-spectrum antibiotic, corticosteroids or immune suppressed states.

Ulcerations over the tongue and bleeding: Stevens-Johnson syndrome.

Invasive candidiasis: Advanced HIV infection/ immunosuppression.

Urine and Feces

Urine volume comes down as a result of dehydration. The urine is concentrated and high colored. Constipation may occur as a result of reduced food intake, dehydration and reduction in physical activity. In typhoid fever and bacterial dysentery diarrhea may occur, always examine urine and feces macroscopically if it is available and mention any

abnormalities noticed along with general examination.

Causes of Fever

1. *Infection:* Commonest cause of fever in all countries, especially developing countries like India is infection. This could be bacterial, viral, rickettsial, chlamydial, protozoal, fungal and helminthic. Almost all infections cause fever as a general reaction.
2. *Inflammatory causes not attributable to infections:* Connective tissue diseases, e.g. systemic lupus erythematosus, rheumatoid disease.
3. *Hypersensitivity reactions: Reaction* to *drugs,* antisera, biological products-serum sickness.
4. *Trauma:* Accidents, blunt trauma and major surgery are accompanied by fever, even in the absence of infective complications.
5. *Extravasation of blood into tissue spaces:* Gives rise to fever.
6. *Neurological disorders:* Lesions in the brainstem may give rise to high fever, e.g. pontine hemorrhage.
7. *Endocrine causes:* Hyperthyroidism, thyroid storm, ovulation.
8. *Physical agents:* Heat hyperpyrexia, post-irradiation fever, dehydration fever in infants and children.
9. *Neoplasms:* Several neoplasms such as hypernephroma and primary carcinoma of the liver give rise to fever as an early manifestation. In acute leukemias and lymphomas fever is a common symptom.
10. Moderate or severe hemolysis and resorption of hematoma from any site may give rise to fever.
11. *Severe muscular effort:* Convulsions, especially status epilepticus, tetanus spasms and severe exercise in closed environments may give rise to fever.
12. *Factitious fever:* Factitious means "produced artificially" and not by a genuine process. Many malingerers pretend illness by manipulating the thermometer so as to record higher temperatures. This is called factitious fever.
13. Very rarely some individuals may have their normal temperature upto 0.5°C above 37°C, with exaggerated circadian rhythm.
14. *Psychogenic fever:* Patients and relatives come with complaint of fever, due to wrong interpretation of the normal body temperature, especially when they are apprehensive of disease. Rarely temperature may be elevated in severe mental stress.

Fever is only a symptom of disease, which should alert the physician to the underlying abnormality. Careful history and physical examination help to identify the cause in many cases. One of the most basic step in evaluation of fever is to ensure that there is high temperature. For clinical purposes fevers of less than one week duration are called short fevers, e.g. short viral fevers, tonsillitis, acute bronchitis and many of the childhood infections.

Fevers that persist for more than two weeks are called prolonged fevers.

Common Causes of Prolonged Fever

Bacterial: Enteric fever, tuberculosis, infective endocarditis, urinary tract infection, rheumatic fever, chronic biliary tract infection, chronic recurrent bacteremias, collection of deep seated pus (subdiaphragmatic, perinephric, pelvic and others), brucellosis.

Protozoal: Malaria, hepatic amebiasis and liver abscess, leishmaniasis, trypanosomiasis.

Helminthic: Filariasis, schistosomiasis, trichinellosis.

Connective tissue diseases: Systemic lupus erythematosus, juvenile arthritis, rheumatic fever.

Viral infection: Acquired immunodeficiency syndrome (AIDS).

Hypersensitivity reaction: Drug allergy, vasculitides

Neoplastic disease: Leukemias, lymphomas, hepatocellular carcinoma, hypernephroma.

Fever of unknown origin (FUO) or Pyrexia of unknown origin (PUO)

Definition of FUO

Documented high body temperature 38.3°C centigrade or higher, lasting more than two to three weeks, with no definite diagnosis, despite proper evaluation, after 3 days of inpatient investigations, or three outpatient visits. Documentation of high temperature should be the first investigation before embarking on detailed evaluation. Viral infections are usually not the cause for FUO because majority of them subside by first week and those viral infections, which persist beyond one week often

have clinical features to suggest the diagnosis. FUO may be classified into:

1. Classic FUO
2. Nosocomial FUO
3. Neutropenic FUO
4. FUO associated with HIV infections.

Causes of Classic FUO (According to Common/ Commonness in Indian Context)

Infections (most cases of FUO are due to infections):

1. Extra-pulmonary tuberculosis
2. Miliary tuberculosis
3. Typhoid fever
4. Malaria
5. Urinary tract infection
6. Pus somewhere (liver abscess, subphrenic, paravertebral, perinephric abscess, splenic abscess, osteomyelitis)
7. Infective endocarditis
8. Brucellosis
9. Infectious mononucleosis
10. Fungal infections
11. Other infections (kala-azar, rickettsial)
12. HIV related infections
13. Meningococcemia
14. Prostatic abscess
15. Pelvic inflammatory disease

Other Uncommon Causes of FUO

a. Rheumatic fever
b. Systemic lupus erythematosus (SLE) and other collagen vascular diseases
c. Leukemias
d. Lymphomas
e. Other malignancies especially liver and kidneys
f. Drug fever
g. Thyrotoxicosis
h. Thromboplebitis
i. Hematoma
j. Thyroiditis
k. Factitious fever

In many cases, the final diagnosis turns out to be underlying tuberculosis, lymphomas or malignancies and collagen vascular diseases.

Cough: When it is present, observe for dry or productive cough its accompliments such as bronchospasm (wheeze), chest pain, dyspnea, position which evokes and gives relief and also characters of the sputum.

LEVEL OF CONSCIOUSNESS

Is the patient conscious and well oriented and is he cooperating with examination, or is he agitated and agressive or having altered level of consciousness. The level of consciousness may change gradually in some metabolic conditions, intracranial infections and space occupying lesions with raised intracranial tension. Loss of consciousness may be abrupt in epilepsy and some cerebrovascular diseases like vertebrobasilar ischemia and intracranial hemorrhage. The patient may have varying grades of altered level of consciousness like, drowsiness, stupor, and coma. Total loss of consciousness from which the patient cannot be aroused is coma. In light coma, the protective reflexes such as withdrawal of a limb due to painful stimuli or pressure on the sternum as well as spontaneous acts like blinking of eyelids, coughing and sneezing are preserved. In deep coma, the patient does not respond to any painful stimuli and sometimes even the brainstem reflexes are lost. Painful stimuli may be applied by pressure over the supraorbital margins of the eyes, pressure over bony points, or pinching the skin. Detailed examination of a comatose patient is given in the Section on Neurology. In all comatose patients, examine for patency of the airways and ensure a patent airway so as to prevent death from asphyxia.

Behavior, Attitude and Posture of the Patient

A patient who is too ill is often uncooperative, self-centred and irritable. As he improves he becomes more cooperative. This fact should be borne in mind by the young physician since extra care may be required to examine such a patient.

Build and Nourishment (Height, Weight, BMI and Other Nutritional Abnormalities)

Build refers to the skeletal frame: *There can be three situations tall, short and of average build.* Height should be recorded with the patient standing without footwear and using a proper scale which measures up to the vertex with his eyes looking forward horizontally. Height of an individual depends upon his genetic characteristics and nutrition in early life. There is considerable variation in height among normal individuals. Short stature *(dwarfism)* is the condition when the height of the individual falls below the third percentile for normal

individuals. Generally, children of tall parents also tend to be tall and *vice versa*. Malnutrition in early life leads to stunting of growth and therefore the height of a person gives important clue to the state of his past nutrition. It is seen that children who are malnourished can catch up if proper nutrition is restored before adolescence is complete. Growth in height ceases with the closure of the epiphyses.

Common conditions which lead to stunting of growth include diseases of early childhood like-general malnutrition, rickets, kyphoscoliosis, tuberculosis and rheumatoid arthritis of the vertebrae, growth hormone deficiency, osteogenesis imperfecta and Paget's disease of bone. Conditions in which there is premature closure of epiphyses such as adrenogenital syndrome and therapy with androgens or corticosteroids in childhood may result in arrest of growth.

The height is abnormally increased in gigantism, Marfan's syndrome and hypogonadism. Gigantism is caused by excessive secretion of growth hormone in early life. In gigantism the growth is proportionate, the axial and peripheral skeletons maintaining their relative proportions. In Marfan's syndrome and hypogonadism there is disproportionate length of the limbs in contrast to the trunk. The hands and are long and slender in Marfan's syndrome (arachnodactyly). In hypogonadism caused by deficiency of androgens the epiphyses do not fuse at normal periods and they remain open. This allows the limbs to grow further and results in disproportionate body features, the limbs being considerably longer compared to the trunk. This configuration is termed *eunuchoid features*.

ANTHROPOMETRY

This consists of measuring the different dimensions with a view to determine the body proportions. In normal persons the arm span (the distance between the tips of the middle fingers when the arms are outstretched at right angles) and the height are more or less equal. The upper segment of the body (distance between the upper border of the pubic symphysis and the vertex of the skull) and the lower segment, (part below the upper border of the pubic symphysis) are also equal. If the arm span exceeds the height by 8 cm or more and the ratio between the upper segment and the lower segment falls below 0.87, it is suggestive of *marfanoid features, eunuchoidism or homocystinuria. Marfan's syndrome* is accompanied by a higher incidence of congenital cardiovascular defects. Hypermobility of the joints occurs in Marfan's syndrome and *Ehlers-Danlos syndrome*. Finger joints, wrist and knee are hyperextensible. arachnodactyly *(spider fingers)* is the condition in which the fingers are long, slender and hyperextensible. In diseases affecting the vertebrae such as kyphoscoliosis, Paget's disease of bone and osteoporosis, the upper segment becomes shorter. In achondroplasia, the trunk and head are normal, but the long bones of the limbs and fingers and toes are shorter.

Abnormalities of the Skull

The shape of the head may vary considerably in health:

1. Abnormally long antero-posterior diameter (dolichocephaly),
2. Abnormally short antero-posterior diameter (brachycephaly).
3. Long and narrow head, skull is deformed and projects like the keel of a boat (scaphocephaly).
4. Head is cone-shaped and pointed (oxycephaly).
5. Head appears to be twisted and lopsided (plagiocephaly)
6. High and pointed skull with wide base (acrocephaly).
7. Triangular head-small pointed forehead with biparietal diameter increased (trigonocephaly).
8. Microcephaly is the condition where the circumference of the head measured over the forehead is less than 35 cm in infants and 52 cm in adults.

Increase in circumference of the head is caused by hydrocephalus in infants and children. Paget's disease of bone leads to increase in head circumference in adults.

The lower level of the hairline at the back of the neck gives clues to disease. In the majority of normal persons the hairline stops at or above the fourth cervical spine. *Low hair line* may be associated with congenital abnormalities of the cervical vertebrae and craniovertebral region, e.g. *Arnold-Chiari malformation, Klippel-Fiel abnormality.* Short stature, short neck, low hairline, head tilt, facial asymmetry, web neck, or scoliosis occur in different combinations in such craniovertebral

Table 2.1: Common congenital abnormalities

Congenital abnormality	*Common associations*
1. Eyes: Micropsia, coloboma of the iris, congenital cataract cardiovascular defects (e.g. PDA)	Congenital rubella syndrome
2. Ears: Abnormalities of the pinna, nerve deafness.	Congenital rubella syndrome cardiovascular defects (e.g. PDA)
3. Hands and feet: Polydactyly (extra fingers or toes) syndactyly defects (fused fingers or toes), lobster fingers and toes (fingers resembling the claws of a lobster)	Congenital cardiac defects
4. Abnormalities of the radius, ulna or both and the hands	Holt-Oram syndrome Congenital cardiac defects (e.g. secundum ASD)
5. Cafe-au-lait spots cutaneous neurofibromata accessory nipples	Neurofibromatosis type-I cardiovascular defects Neurovascular abnormalities
6. Angiomatous malformations over the face or the trunk	Angiomatous malformation in the brain or spinal cord

junction anomalies. Anthropometry also helps to distinguish racial features among population groups.

Congenital Abnormalities

Congenital abnormalities are seen approximately in 21 out of 1000 live births. Many of these are associated with other more serious congenital disorders. Detection of these abnormalities lead to early recognition of other systemic abnormalities as well. The more common congenital abnormalities which can be easily picked up on general examination are listed in Table 2.1.

There are several other well-established associations between obvious congenital abnormalities and systemic defects. It is not possible to list all the congenital malformations and their systemic associations in this volume. Detection of any congenital abnormality on general examination should alert the physician to the coexistence of a more serious systemic abnormality.

WEIGHT AND NUTRITION

A weighing machine should always be available in the examination area or consulting room. The weight should be recorded using a properly serviced balance whose accuracy should be calibrated at regular intervals. It is ideal to record the weight with light clothes without footwear, under the same conditions at every visit. Variations upto 1 kg may occur as a result of ingestion of food, filling of urinary bladder and the colon. Variations beyond this range should draw the attention of the physician.

Weight of an individual represents the state of current nutritional status. In a healthy individual the weight remains more or less steady from the age of 30 to 65 years after which it may tend to fall gradually. In many diseases such as diabetes mellitus, thyrotoxicosis, tuberculosis, malignancies, and psychiatric disorders there is significant loss of weight. As these conditions improve with treatment the weight returns to normal. Unexplained loss of weight by 5 to 10% should evoke suspicion about serious underlying disease necessitating prompt evaluation.

Weight in excess of 10% of the ideal body weight caused by excessive deposition of fat is termed *obesity* and is abnormal. Physiological increase in weight occurs during periods of growth and pregnancy. Pathological increase in weight can occur as a result of fluid retention and in myxedema. In obesity the gain in weight is gradual, occurring over several months or years. Fluid retention leads to rapid increase in weight, often in excess of 1 kg/day. The importance of recording the weight at every visit of the patient cannot be over-emphasised. The *body mass index* (BMI) is accepted as a reliable parameter to diagnose obesity.

$$\text{BMI} = \frac{\text{Weight in kg}}{(\text{Height in meters})^2}$$

The BMI is normally 18 to 23. Above 25 suggests obesity in women and above 30, in men. Higher values of BMI indicate the severity of obesity (Table 2.2). Other parameters employed to define the severity of obesity and malnutrition are mid armcircumference, skin fold thickness and waist-hip ratio.

Nutrition

Whereas build refers to the skeletal frame, nutrition refers to the soft tissue compartment of the body. In nutrition primarily there are three situations like moderately nourished, obese and emaciated; in addition other specific nutritional deficiencies noted have to be mentioned. Undernutrition leads to loss

Table 2.2: Classification of overweight and obesity by BMI, waist circumference and associated disease risk

	BMI kg/m²	*Obesity class*	*Disease risk* relative to normal weight and waist circumference*	
			Men ≤ 102 cm (≤ 40 in)	*> 102 cm (> 40 in)*
			Women ≤ 88 cm (≤ 35 in)	*>88 cm (> 35 in)*
Underweight	<18		-	-
Normal	18.5–23		-	-
Overweight	23.5–29.9		Increased	High
Obesity	30–34.9 35–35.9	I II	High Very high	Very high Very high
Extreme obesity	≥ 40	III	Extremely high	Extremely high

* Disease risk for type 2 diabetes, hypertension, and CVD.
Increased waist circumference can also be a marker for increased risk even in persons of normal weight. *Reproduced:* From Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults—The Evidence Report. National Institutes of Health. Obes Res 1998;6:515

of weight and emaciation. The skin is wrinkled and body fat is reduced.

Obese individuals show excess deposition of fat over the trunk, abdomen, gluteal regions and limbs. They are more likely to suffer from hypertension and ischemic heart disease.

The combination of abdominal obesity with metabolic risk factors such as hyperglycemia and dyslipidemia and hypertension is termed "metabolic syndrome"

Though BMI used to be considered as a major determinant of obesity – related complications, it is seen that in peoples of Indian and South East Asian origin, several other parameters such as the waist-hip birth are even more important. For standard Indian subjects, BMI > 25 is taken to denote obesity.

Acanthosis nigricans is a common finding seen is persons with metabolic syndrome. It consists of thickening, coarseness and pigmentation of the skin around the neck, especially at the back and other flexural areas (Fig. 2.10)

Nutrition refers to the sum total of the processes of ingestion and utilization of food substances by which growth, repair and maintenance of body functions are achieved. Proper nutrition depends upon the optimum intake of carbohydrates, proteins, fats, vitamins, minerals and water. Well nourished individuals are alert, active, with normal heights



Fig. 2.10: Acanthosis nigricans. *Note:* Thickened, coarse and pigmented skin

and weights and free from any sign of nutritional deficiencies. Nutritional deficiencies account for considerable morbidity and mortality in developing countries. Therefore, it is important to look specially for evidences of malnutrition. Since nutritional requirements are higher during periods of growth and pregnancy, children and pregnant women are likely to be affected more by malnutrition. Elderly individuals are also likely to suffer due to poor earning capacity, neglect, social deprivation and loss of teeth. Usually nutritional deficiencies do not occur in isolation. In many cases several deficiencies coexist. Malnutrition predisposes to all infections since the immune status of the individual is impaired.

Deficiency of Nutrients—Major Signs

Calories (starvation)	Marasmus in children, stunted growth, delayed milestones in children, delayed puberty, emaciation
Proteins	Nutritional edema, Kwashiorkor in children, anemia
Fats	Fats contribute to the total caloric needs. Deficiency of fat soluble vitamins (A,D,E and K) may develop if all the dietary sources are eliminated. But this is very unusual in normal setting
Vitamin A	Night blindness, xerophthalmia keratomalacia, corneal ulceration, blindness, propensity to develop frequent respiratory infections
Vitamin D	Rickets in children, osteomalacia in adults, tetany
Vitamin K	Hemorrhagic tendencies
Thiamine (Vitamin B_1)	Polyneuropathy, myocarditis, beriberi, Wernicke's encephalopathy
Riboflavin (Vitamin B_2)	Angulostomatitis, glossitis, circumcorneal congestion, genital lesions

Contd...

Contd...

Niacin (Vitamin B_3)	Glossitis, dermatitis over areas exposed to sunlight, mental changes, diarrhea
Biotin	Deficiency is more in infants. Lassitude, irritability, paraesthesia, anorexia
Pyridoxin (Vitamin B_6)	Peripheral neuropathy, rashes, hair loss, dermatitis, cheliosis, angulostomatitis, glossitis, infantile convulsions
Ascorbic acid (Vitamin C)	Bleeding gums, follicular keratosis over skin and follicular hemorrhages, delay in healing of wounds, tendency for infections, scurvy
Pantothenic acid	Possibly neuromuscular degeneration, dermal and hair changes
Folic acid	Megaloblastic anemia
Vitamin B_{12}	Megaloblastic anemia, subacute combined degeneration of spinal cord, mental changes
Minerals Iron	Iron deficiency states, iron deficiency anemia, koilonychia, sideropenic dysphagia
Calcium	Hypocalcemia, tetany, osteomalacia
Iodine	Goiter, goitrous cretinism in the newborns and children, several iodine deficiency disorders
Magnesium	Tetany, cardiac arrhythmias

PALLOR

Pallor due to low hemoglobin is usually detected by examination of the palpebral conjunctiva of the lower eyelid (Fig. 2.11). Normal color of the skin depends on the degree of pigmentation and the vascularity of the part. The mucous membranes and nails are normally pink and their color depends upon the amount of hemoglobin in the circulating blood. Pallor of mucous membranes is mainly due to anemia. The severity of pallor and the severity of anemia may not correlate directly in all cases. For assessing the severity of pallor, the conjunctiva, tongue, oral mucosa, palm and hard palate have to be examined in good light. The mucosa over the hard palate reflects more closely the hemoglobin status. The diagnosis of anemia should always be confirmed by estimation of hemoglobin (Fig. 2.12).

JAUNDICE

Jaundice is yellow pigmentation of the sclera, skin, mucous membranes and other tissues caused by excess of circulating bilirubin. Normal level of serum bilirubin is up to 1 mg/ dL. The presence of scleral icterus indicates a serum bilirubin of at least 3.0 mg/dL. Bilirubin attaches to collagenous tissue easily and therefore tissues rich in collagen are stained most. After elevating the eyelids ask the patient to look down, and examine the sclera above the cornea, which is covered by the upper eyelid (Figs 2.13 and 2.14). For identifying mild jaundice the patient should be examined in daylight. Jaundice is best appreciated over the upper part of the sclera, under surface of the tongue, palms, nails and skin. It is best seen in upper sclera as there is more collagen, Also, bilirubin in the sun exposed areas of sclera gets photo oxidized to water soluble bilirubin which gets washed away by the blood or tear film. When the jaundice is severe, almost all tissues are stained yellow. In the setting of recent onset severe hepatocellular damage as in acute viral hepatitis or toxic hepatitis, the sclera may not show jaundice, because staining of tissues by excess bilirubin takes 2 to 3 days. Therefore, it is a golden rule to look at the color of urine and examine urine for bile pigments and the patient repeatedly on successive days for jaundice if a likely cause is suspected (Fig. 2.15).

Chronic obstructive jaundice gives rise to a greenish yellow tinge to the sclera. Pruritus is characteristic of obstructive jaundice. It is therefore, important to look for scratch marks in jaundiced patients. Hemolytic jaundice is associated with pallor and mild lemon yellow jaundice in severe cases. If there is presence of severe jaundice in



Fig. 2:11: Examination for pallor



Fig. 2.12: Pallor in a patient with severe anemia



Fig. 2.13: Leptospirosis with jaundiced coated tongue



Fig. 2.14: Examining for jaundice



Fig. 2:15: Thalassemic patient with typical facial appearance and jaundice

hemolytic anemia it may be due to coexistent hepatic dysfunction, pigment gallstones or may indicate hemolytic crises. In hemolytic jaundice urine does not generally contain bile pigments, since unconjugated bilirubin does not appear in urine-(acholuric) jaundice. In carotinemia the skin may have a yellowish tinge but the sclera is not affected. It is the yellow color imparted to the skin by the presence of carotene; it occurs in healthy individuals who ingest excessive amounts of vegetables and fruits that contain carotene, such as carrots, leafy vegetables, squash, peaches, and oranges but usually seen in those with coexisting hypothyroidism. Drugs like clofazimine, quinacrine, and rifabutin may stain the skin yellow to reddish brown. Stigmata of chronic liver disease, including spider nevi, palmar erythema, gynecomastia, caput medusae, parotid gland enlargement, and testicular atrophy are commonly seen in advanced alcoholic cirrhosis and occasionally in other types of cirrhosis. An enlarged left supraclavicular node (Virchow's node) or periumbilical nodule (Sister Mary Joseph's nodule) suggests an abdominal malignancy. Jugular venous distention, a sign of right-sided heart failure, suggests hepatic congestion as the cause for jaundice. Vitamin B_{12} and folate defeciency may lead to jaundice due to ineffective erythropoesis. Associated, muscle tenderness, sub conjunctival hemorrhage and renal dysfunction may point to a diagnosis of leptospirosis. Recurrent jaundice may occur with Gilbert's syndrome, malaria, G6PD deficiency and chronic active or alcoholic hepatitis.

Gilbert's syndrome is a genetically transmitted disease caused by deficiency of microsomal UDP glucoronyl transferase which is needed to convert unconjugated to soluble conjugated bilirubin. The jaundice is generally mild (bilirubin < 6 mg/dL) and stigmata of chronic liver disease do not develop.

CYANOSIS

This is bluish, or dark purple coloration of the skin and mucous membranes caused by the presence of excessive amounts of reduced hemoglobin in arterial blood. For cyanosis to become visible the amount of reduced hemoglobin should exceed 5g/dL. In severely anemic patients since this level of reduced hemoglobin cannot be reached, cyanosis

may not develop even when there is hypoxemia. The opposite is true of polycythemia in which cyanosis may be present even under ordinary conditions. Cyanosis may be due to central causes or peripheral causes. Mixing of arterial and venous blood at the level of the heart or great vessels, due to shunts and defective oxygenation in the lungs, give rise to central cyanosis. In central cyanosis, the central parts of the body such as the tongue as well as the peripheral parts such as the nail beds, tips of fingers and toes and the tip of the nose are cyanosed. The extremities are warm. Central cyanosis is seen characteristically in congenital cyanotic heart disease, chronic bronchitis emphysema and other pulmonary diseases impairing gas exchange in the alveoli. Inhalation of pure oxygen does not correct the cyanosis in the case of congenital heart disease. In the case of pulmonary diseases, unless the lesion is far advanced inhalation of oxygen helps to correct the cyanosis partially. Central cyanosis is associated with the development of secondary polycythemia (Fig. 2.16).

Peripheral cyanosis denotes the condition where the extremities (tips of fingers and toes, nail beds and tip of the nose) are cyanosed, while the central parts like the tongue are not. Unlike as in central cyanosis the extremities with cyanosis are cold to feel. The mechanism of cyanosis is peripheral like arterial obstruction or vasospasm. Warming the part may relieve the cyanosis if it is vasospasm. Peripheral cyanosis is caused by excessive extraction of oxygen by the tissues from the capillaries when there is sluggish flow of blood due to any cause including reduction in cardiac output. Sometimes dark pigmentation of the tongue and oral mucosa may resemble central cyanosis. In such cases, the peripheries are not blue. On pressing with a glass slide over the tongue, if the tongue blanches and the part becomes pale, it suggests cyanosis. In pigmentation there is no change on applying pressure. Presence of excess of methemoglobin or sulphemoglobin leads to bluish or leaden color resembling cyanosis. Most often this is caused by taking drugs or chemicals which alter the color of hemoglobin, e.g. dapsone, nitrates, marking ink, dyes and chemicals. A cherry-colored flush, rather than cyanosis, is caused by carboxyhemoglobin (COHb). Arterial obstruction to an extremity, as with an embolus (Fig. 2.17), or arteriolar constriction, as in cold-induced vasospasm (Raynaud's phenomenon) generally results in pallor and coldness first followed by cyanosis confined to the area affected. Venous obstruction, as in thrombophlebitis, dilates the subpapillary venous plexuses and thereby intensifies cyanosis. Differential cyanosis occurs in patents with Eisenmenger syndrome with patent ductus arteriosus (PDA)—the lower extremities are cyanosed where as the upper extremities are not.



Fig. 2.16: Central cyanosis and polycythemia in patient with COPD and respiratory failure (blue bloater)



Fig. 2.17: Cyanosis of index and small fingers plus clubbing in infective endocarditis with embolism

CLUBBING OF FINGERS

In normal subjects the level of the proximal margins of the nail is slightly lower than that of the nail fold when examined from the side. There is a rhomboid space between the two thumb nail beds when both the thumbs are kept against each other (Shamroth's sign Fig. 2.18). In several conditions the tissues in the nail bed and finger pulp hypertrophy giving rise to convexity of the nail and nail bed. This is called clubbing (Fig. 2.19). In advanced cases the nails and finger tips assume drumstick appearance. Clubbing should be examined by inspecting the finger tip from the side keeping the finger horizontally at eye level. When clubbing occurs the Shamroth's sign disappears.

In many cases the toes and fingers are affected together and both sides are symmetrically involved. Clubbing may evolve rapidly within 2 to 3 weeks as in empyema or lung abscess or may develop slowly over years as in congenital cyanotic heart disease. Unilateral clubbing of the upper limbs may develop in aneurysm of the ipsilateral subclavian artery. Clubbing recedes when the underlying lesion is cured. At times persons whose occupations lead to repeated minor trauma to the fingertips develop clubbing, e.g. carpenters and masons. This has no pathological significance.

Clubbing can be graded as given below:

Normal finger tip: The nail joins the nail bed at an angle.

Grade I: The nail-bed becomes more fluctuant than normal, but can be seen in normal individuals also.

Grade II: Obliteration of the angle between the nail and nail-bed.

Grade III: Bulbous appearance of the nail and finger tip (parrot beak apperance).

Grade IV: Fingertips as in the third degree, but in addition, painful thickening of the ends of long bones of the limbs also develop. This is called hypertrophic *pulmonary osteoarthropathy.* This occurs more frequently in lung diseases such as adenocarcinoma lung and suppurative lung conditions.

Though in a few persons clubbing may be present as a familial trait, in the vast majority its presence indicates disease.

More Common Causes

Cardiovascular system: Cyanotic congenital heart disease, infective endocarditis Fig. 2.19.

Respiratory system: Bronchiectasis, lung abscess, bronchogenic carcinoma, empyema, pulmonary interstitial fibrosis, etc.

Less Common Causes

Cirrhosis of liver, carcinoma liver, granulomatous disease of the intestines (Crohn's disease and ulcerative colitis) and Graves' disease (primary exophthalmic goiter).

Nail Changes

Koilonychia (Fig. 2.20): The nails are flattened, brittle and in more advanced cases, spoonshaped.



Fig. 2.18: Normal appearance Shamroth's sign



Fig. 2.19: Clubbing in a patient with subacute bacterial endocarditis



Fig. 2.20: Koilonychia and pallor



Fig. 2.21: Splinter hemorrhage in nails

Both toe nails and finger nails may show this change, the former being affected earlier. Koilonychia is almost always suggestive of severe iron deficiency state. The condition subsides when the deficiency is rectified. Nail may be brittle with cracked edges or may be flat (*platonychia*) in early iron deficiency anemia. This is very important as iron deficiency can be diagnosed in early stages and proper treatment can be initiated. Angular stomatitis—fissures at the corners of the mouth is another manifestation of severe iron deficiency anemia.

Whitish discoloration of the nail (leuconychia): Small white patches on the nail may be seen in normal persons. White bands on the nails may indicate hypoalbuminemic states like chronic liver disease or nephrotic syndrome.

Splinter hemorrhages in the nail-beds (Fig. 2.21): These are seen in infective endocarditis and certain forms of vasculitis like polyarteritis nodosa, vasculitis associated with scleroderma, rheumatoid arthritis, etc.

Fungus infection of the nails may make them thick, rough and distorted (onychomycosis). Pitting of the nails and sometimes onycholysis (separation from nail bed) occurs in psoriasis. Onycholysis can occur due to candidal infection also. Nails may fail to develop normally in genetic disorders such as nail-patella syndrome.

Brittle nails develop due to external causes like solvents, detergents and soaps. Soaps cause weakening of nail edges, splitting and softening. Transverse ridging is called *Beau's lines* which develop due to arrest of growth during a period of serious illness followed by recovery of growth. Multiple longitudinal ridging is constitutional. In chronic renal failure, the nails may show pallor (whitening) of the proximal half and reddish or brownish pigmentation of the distal half "half and half nail". Impaired peripheral circulation, especially of the lower limbs as in arterial occlusion and neurological disorders such as nerve root compression by disk prolapse may lead to thinning, longitudinal ridging and onycholysis.

SKIN

The skin closely mirrors several systemic disorders. Skin should be examined under day light or bright illumination. Normal skin is smooth, lustrous, uniformly pigmented and having normal distribution of hairs. Skin color depends upon the pigmentation and vascularity underneath. When pinched up and released, normal skin resumes the original shape without leaving any wrinkles. Detailed description is given in Section 15.

Look for changes in color, texture and distribution of hair. Loss of elasticity and wrink-ling may occur in the elderly, but if it occurs in the younger age groups, it should suggest rapid loss of weight or dehydration. Hyperelasticity (ability to be pinched up freely) occurs in conditions like Ehlers-Danlos syndrome where the structure of collagen is abnormal. Particularly look for rashes, parasites such as head louse, body louse and pubic louse, ticks, mites, scabies, pigmentary disturbances such vitiligo, 'cafe au lait' spots, hyperpigmentation fungal infections of the skin and nails, neurofibromata, nevi, hemangiomas and eschars (Figs 2.22 and 2.23). Eschars are necrotic ulcers, often painless and unnoticed by the patient,



Fig. 2.22: Hyperpigmentation of knuckles and pallor in megaloblastic anemia



Fig. 2.23: Adenoma sebaceum in tuberous sclerosis

produced as a result of bites of ticks or mites seen in the skin folds-such as groin, intergluteal region, submammary regions or axillae. Presence of eschar may give clue to arthropod borne infections. *Campbell- de-Morgan spots* are small red areas seen most over the trunk and abdomen. They are benign and do not have any pathological association.

Skin is the largest organ in the body and it can reflect various systemic diseases, for example:

1. Erythroderma (reddish discoloration of majority of skin surface)—drug induced (penicillins, sulfonamides, carbamazepine, phenytoin) or may be part of cutaneous T cell lymphoma (Sézary syndrome).
2. Alopecia (loss of hair)—associated with SLE, hypothyroidism.
3. Telangiectasia—associated with hereditary hemorrhagic telangiectasia (Osler Weber Rendu disease) or ataxia telangiectasia
4. Vitiligo (hypopigmented patches)—associated autoimmune disorders.
5. Acanthosis nigricans (hyperpigmentation and rough velvety looking skin in neck and flexural areas)–associated with metabolic syndrome, Insulin resistant diabetes, internal malignancy, Cushing's syndrome, obesity.
6. Seborrheic keratoses—sudden appearence with skin tags and acanthosis may suggest internal malignancy (sign of Leser-Trélat).
7. Hyperpigmentation—may be associated with hemochromatosis, Addison's disease or vitamin B_{12} and folate defeciency.
8. Papulonodular skin lesions—may be associated with neurofibromatosis, cutaneous lupus, Sweet's syndrome (neutrophilic dermatosis) or leukemia cutis.
9. Xanthoma—associated with hyperlipidemia.
10. Xanthelasma—at times associated with dyslipidemia (this relation is very weak)
11. Necrobiosis lipoidica (yellow colored papules primarily on shins)—associated with diabetes.
12. Tophi (yellow firm lesions on helix of ear, olecranon due to monosodium urate crystal deposition)—associated with gout.
13. Petechiae/purpurae/ecchymosis (bleeding into skin)—associated with thrombocytopenia due to ITP or leukemia and other platelet disorders.
14. Palpable purpura—associated with vasculitis.
15. Oral ulcers—associated with Behcet's disease, SLE or Stevens Johnson syndrome.

Pyoderma gangrenosum (ulcers with undermined edges and erythematous halo)—associated with inflammatory bowel disease or rheumatoid arthritis.

Further details of physical examination of skin are given in Section 15.

HAIR DISTRIBUTION

In the males, with the onset of puberty hair grows over the face (beard area) and body in a characteristic distribution. In both sexes hair grows over the genitalia and axillae. The term alopecia refers to loss of hair. Alopecia may be localized-alopecia areata or generalized-alopecia totalis. Occurrence of alopecia may be rapid as in alopecia areata or gradual as in normal aging, hypothyroidism or fungus infections. Local causes include alopecia areata, tinea capitis, trichotillomania, burns and local trauma. Systemic lupus erythematosus, myxedema, sarcoidosis and malnutrition may give rise to generalized hair loss. In these conditions if the hair root is not damaged, the hair can regrow. If



Fig. 2.24: Absence of body hair, axillary hair in hypogonadism and cirrhosis due to hemochromatosis in 28 years old male



Fig. 2.26: Note the excessive hair growth over the face and moustache area. Often the whole body is affected (Hirsuitism)



Fig. 2.25: Female pattern pubic hair in the same patient in Fig. 2.24

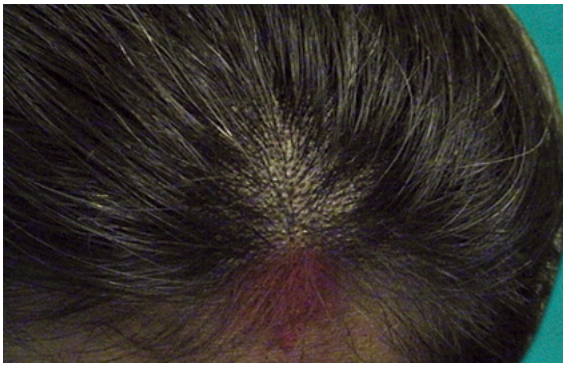


Fig. 2.27: Premature graying in 20 years old with B_{12} deficiency

the hair root is destroyed, the baldness becomes permanent. Alopecia may involve not only the scalp, but all parts of the body. Administration of anticancer drugs is a common cause of temporary hair loss at all ages.

Failure of hair growth over the genitalia and face should suggest hypogonadism (primary or secondary) (Figs 2.24 and 2.25).

When an adult male develops hypogonadism the facial and the body hair may be lost. Hair loss or absence of hair in the axillae and pubic region suggests hypopituitarism. Systemic diseases like cirrhosis liver and lepromatous leprosy and therapy with estrogens may lead to loss of facial and body hair in males.

Excessive hair over the face and body in women is called hirsuitism (Fig. 2.26). This occurs in conditions where there is excessive androgen secretion. Frontal baldness is a normal phenomenon in men and with age the extent of baldness increases. Baldness in women should suggest the possibility of hyperan-drogenism or hyperadrenal corticism. Abnormal frontal baldness develops in dystrophia myotonica.

Graying of hair is a natural process most frequently associated with aging. In some cases grey hair develops even in young. Rapid depigment ation of the hair may develop in severe protein malnutrition. B_{12} deficiency is a cause for premature graying of hair (Fig. 2.27).

EDEMA

Clinical Examination

Excessive accumulation of fluid in interstitial tissue spaces is called edema. Edema may be generalized or localized. In generalized edema (syn. dropsy, anasarca) there is retention of excessive fluid in

tissues resulting in increase in total body fluids. This excessive fluid is due to transudation of fluid into the tissue spaces, increase in fluid in cells and increase of fluid volume in the venous and capillary sides of the circulation. Along with the retention of water, there is retention of sodium and chloride.

Generalized edema results in rapid increase in weight (more than 500–1000 g daily), oliguria (urine volume falling below 400 mL*I*day) and accumulation of fluid in all tissues.

In edema, the patient complains of tightness of the part and unusual heaviness. The skin is stretched and shiny and the normal wrinkles are obliterated. Superficial veins become less prominent. *The confirmatory sign of edema* is *pitting on pressure*, i.e. pressure over the edematous part displaces the fluid and this leads to the formation of a dimple. The test is performed by exerting gentle pressure with the flat of the thumb for ten seconds over a bony area (shin of the tibia, medial malleolus, and sacrum), and looking for pitting (Figs 2.28A and B).

Generalized Edema

Causes of Generalized Edema

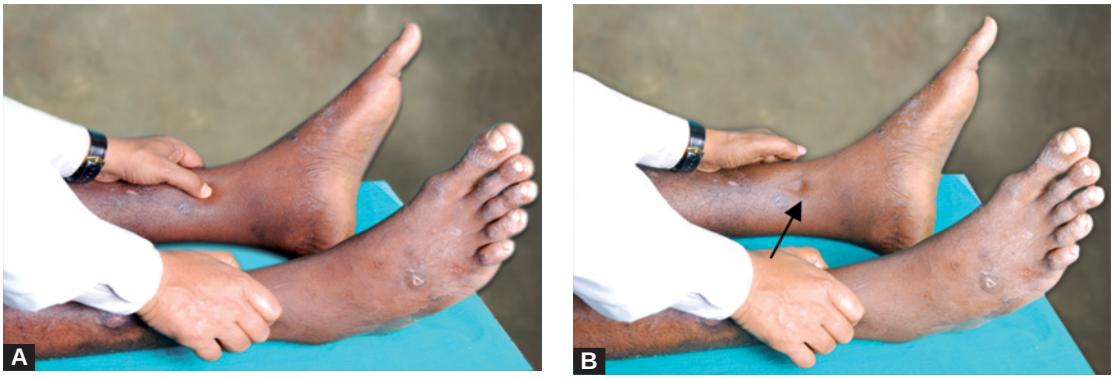
Cardiac failure: In right-sided heart failure there is systemic venous congestion and generalized edema. The edema is dependent in nature, i.e. edema is most prominent in those parts which are the lowest. In ambulant subjects the edema is maximal over the ankles and feet (pedal edema) and it is worse towards the end of day. It clears up with recumbency. In bedridden patients edema is most prominent over the sacrum. An early symptom of generalized fluid retention is nocturnal polyuria. The fluid which accumulates during the day is cleared at night due to improvement in cardiac output. As the condition progresses, the edema becomes established at all times. With diuretic therapy the urine volume increases and the edema clears. Cardiac edema is accompanied by other signs of cardiac failure such as exertional dyspnea, engorged jugulars and hepatic enlargement. In the early stages of left-sided heart failure, pulmonary congestion and pulmonary edema occur. Later right heart failure supervenes and generalized edema develops.

Renal causes: Generalized edema is a common accompaniment of acute nephritic syndrome and nephrotic syndrome. In acute nephritic syndrome, the edema is most prominent over the eyelids and face, especially on waking up after sleep. In nephrotic syndrome, the edema is caused by hypoalbuminemia and it is also dependent in nature.

Hypoalbuminemia: Serum albumin accounts for the major part of colloid osmotic pressure of the plasma, which is responsible for drawing the fluid from the tissue spaces into the venous end of the capillaries and lymphatics. Normal level of plasma albumin is 3.5 to 5 g/dL. When the level of plasma albumin falls below 2.5 g/dL the fall in oncotic pressure leads to failure of reabsorption of fluid from the tissues into the circulation and consequent accumulation in tissue spaces. This type of edema is also dependent in nature.

Chronic liver disease with hypoalbuminemia leads to generalized edema.

Beriberi **(**due to thiamine deficiency***)*** *can lead onto congestive cardiac failure (CCF) with generalized edema.*



Figs 2.28A and B: (A) Demonstration of pitting on pressure, (B) Pit caused by pressure (arrow)

Localized Edema

Unlike as in generalized edema, there is no accumulation of fluid in the entire body but there is accumulation in localized area with edema confined to that region.

Causes of Localized Edema

Inflammatory edema: Edema and swelling are integral constituents of inflammation. Due to several factors (both cellular and humoral) there is congestion of the vessels, increased permeability of the capillaries leading to the exudation of large amount of protein-rich fluid and cells into the tissue. This protein-rich fluid raises the osmotic pressure of tissue fluid, thereby offering resistance to reabsorption into the capillaries. In generalized edema, the edematous parts are not tender. Inflammatory edema is warm to touch, the overlying skin is erythematous and it is tender.

Obstruction to blood vessels or lymphatics: Venous obstruction results in rise in capillary pressure distal to the occlusion. This leads to transudation of greater quantities of fluid. Similarly lymphatic occlusion also leads to edema distal to the occlusion. Lymph being rich in protein, tends to increase the osmotic pressure of the edema fluid.

Reduction of tissue tension: Normal skin and subcutaneous tissue which are rich in collagen exert a constant elastic tension which prevents free eggress of fluid into the interstitial compartment. Atrophy of the skin, subcutaneous tissue and fat which occurs in emaciation and old age leads to fall in tissue tension and this favors the accumulation of excess of tissue fluid. If edema persists for a long duration it tends to get organized with proliferation of fibroblasts. At this stage, it is firmer and does not readily pit on pressure, e.g. filarial edema.

Lymphedema: Results in the accumulation of fluid in the skin and subcutaneous tissue. There is general thickening and induration of the skin. On pinching, the skin assumes the appearance of an orange peel (peau-de-orange appearance).

When generalized edema is advanced, ascites and pleural effusions may develop. The fluid is a transudate. With clearance of the edema, the effusions also clear. In cirrhosis of the liver, in addition to hypoalbuminemia, there is portal hypertension and this factor tends to localize the fluid to the abdominal cavity particularly.

LYMPH NODES

There are around 400 to 450 lymph nodes in an young adult. They are normally just palpable as small firm nontender masses less than 0.5 cm in diameter especially in children or they are not palpable at all. In several diseases pathologically the lymph nodes enlarge and become palpable and visible (Fig. 2.29).

Significance of lymphadenopathy: Any palpable lymph node anywhere in the body is a diagnostic problem. In general nodes larger than 2 cm, any lymph node in the supraclavicular region, scalene node, any generalized lymphadenopathy, hard and fixed nodes are all significant. Equally important is the clinical setting to decide significance or lack of significance of lymphadenopathy. Lymph node enlargement may be due to diseases primarily affecting the lymph nodes as in lymphoma, lymphatic leukemia, tuberculosis and lymphogranuloma venereum or may be secondary to disease in their areas of drainage. The former could be generalized whereas the latter is always localized.

Location of Lymph Nodes and their Areas of Drainage

Neck: Lymph nodes may be broadly divided into superficial and deep groups with reference to their relation with the deep fascia. Superficial group consists of the occipital, retro-orbital, parotid, buccal, submandibular, submental and anterior and posterior cervical nodes. Supraclavicular nodes are situated above the medial ends of the clavicles. Pretracheal (scalene) nodes are situated behind the origin of the sternal head of the sternocleidomastoid muscle, usually palpated in between the two heads of this muscle.



Fig. 2.29: Tuberculous lymphadenopathy with caseation necrosis neck

Groups of nodes	*Drainage area*
Occipital	Occipital scalp and back of neck and retro-orbital area
Parotid (preauricular)	Face (posterior)
Buccal	Face, anterior and upper lip, tongue, floor of mouth, lower jaw
Submandibular	Lower lip, tip of tongue, central part of floor of mouth
Upper anterior cervical	Nose, mouth, pharynx, upper larynx and tonsil
Lower posterior (supraclavicular)	Lower neck, upper chest and afferents from axilla and mediastinum
Scalene node right	Right lung and lower parts of left lung, mediastinum
Scalene node left	Upper parts of left lung, mediastinum

The term *Virchow's nodes* is given to the group of supraclavicular nodes which are situated between the two heads of sternocleidomastoid on the left side. They enlarge due to metastatic deposits from malignant lesions involving stomach, testes and other abdominal viscera.

Upper limb—axillary nodes: These consist of the lateral, anterior, posterior, central and apical groups.

Lateral	*Upper limb*
Anterior axillary	Supraumbilical portions of anterior and lateral parts of the trunk and mammary gland
Posterior (scapular) axillary placed on posterior wall	Skin and superficial muscles of the inferior and posterior parts of the neck and dorsal aspects of the trunk above the iliac crest
Central axillary placed (placed deeply in the axillary fat)	Drain all areas
Apical (extending to the apex of the axilla)	Drain the mammary gland and lymph from other groups
Supratrochlear nodes placed along the basilic vein above the cubital fold	Medial aspects of the forearm and wrist
Inguinal nodes	
Superficial group	Lower abdominal wall and upper part of the thigh
Deep horizontal	External genitalia, perineum and efferents from superficial group
Deep vertical	Lower limbs and efferents from superficial group
Iliac group situated along the iliac vessels	
External iliac	Efferents from inguinal groups
Internal iliac	Uterus, rectum, bladder
Popliteal group embedded in the popliteal fossa	Leg

Intra-abdominal nodes: These occur in relation to abdominal organs. Several groups are recognizable: pyloric, splenic, porta hepatis, mesenteric and others. They lie in relation to major vessels which supply viscera viz. branches of coeliac axis and superior and inferior mesenteric vessels. Efferents from these drain to the retroperitoneal (para aortic) nodes.

Some important nodes to remember	*Groups of lymph nodes enlarged*
Lesions of the scalp	Occipital, postauricular
Larynx, vocal cords and tonsils	Upper deep cervical
Oral cavity	Submental, submandibular
Lungs	Tracheo-bronchial, mediastinal and scalene.
Breasts	Axilla, (anterior, central, apical) internal mammary group and supraclavicular Esophagus
Upper third	Lower cervical
Middle third	Paraesophageal and tracheobronchial gastric
Lower third	
Stomach	
Fundus	Splenic, left gastric
Pylorus	Supra and sub-pyloric groups
Pancreas	
Head	Sub-pyloric group
Other parts	splenic group
Testes	Para aortic, supraclavicular
Ovaries	Para aortic, supraclavicular
External genitalia in male	Inguinal, iliac
External genitalia in female	Inguinal, Iliac

Method of Palpation of Lymph Nodes

Submandibular and submental nodes: Palpate with the tip of the finger gently introduced underneath the mandible and moved from side to side. Can be palpated form the front or while standing behind the patient.

Cervical nodes: Stand behind the patient. With the palm of the hand and the fingers palpate the nodes, with the patient's neck flexed and turned to the side so as to relax the sternomastoid (Figs 2.30 to 2.32).

Supraclavicular nodes: Palpate over the medial ends of the clavicles above the origin of the sternocleidomastoid (Fig. 2.33).

Pretracheal nodes (scalene nodes): Flex the neck to relax the sternomastoid, palpate gently deep behind the sternocleidomastoid muscle and in between the two heads of it. This procedure is slightly uncomfortable (Figs 2.33 and 2.34).

Axillary nodes: Explain the procedure to the patient. Standing in front, gently insert the palm of the hand into the axilla while the other hand holds



Fig. 2.30: Palpating submental nodes and submandibular nodes



Fig. 2.33: Palpating scalene nodes, method-1



Fig. 2.31: Palpating cervical and supraclavicular lymph nodes



Fig. 2.34: Palpating scalene nodes, method-2

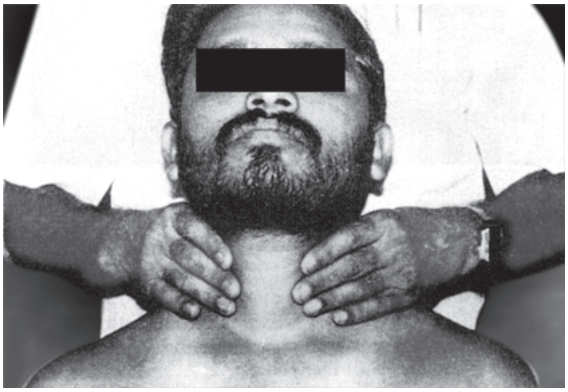


Fig. 2.32: Palpitating anterior cervical lymph nodes

the arm ensuring that its weight is supported on the examiners arm and manipulates it so as to relax the axillary floor. The nodes are systematically palpated in the apex and anterior, medial, lateral and posterior portions of the axilla and infra axillary region of the chest. The right hand of the examiner may be used to palpate the left axilla and the left hand to palpate the right axilla (Fig. 2.35).

Supratrochlear nodes (Epitrochlear nodes): Lift the arm and flex the elbow to a right angle. Palpate the nodes with the flat of the thumb alone or index, middle and ring fingers together by gentle movement up and down (Fig. 2.36).

Inguinal nodes: When the patient is lying supine or standing with thigh flexed to 10°, palpate with the palmar aspect of the fingers.

Popliteal nodes: Flex the knees and palpate deep by introducing the fingers into the popliteal fossa.

Abdominal lymph nodes: These can be identified as discrete nodular or matted masses in the abdomen



Fig. 2.35: Palapating right axillary nodes



Fig. 2.36: Palpating for right supratrochlear (epitrochlear) node

on deep palpation (details of abdominal palpation are given in Section 3).

Mediastinal lymph nodes: Enlargement of the nodes may be identified in some cases by percussing the chest to detect widening of the dullness over the upper mediastinum. Further confirmation can be made by radiography and CT scanning.

Points to be Noted while Examining Lymph Nodes

- Site
- Size of the largest and smallest gland
- Number of nodes enlarged
- Consistency (soft, firm or hard)
- Tenderness
- Mobility
- Matted or discrete
- Fixity to skin and condition of the overlying skin
- Generalized or localized
- Adjacent groups of nodes
- Lesions in the areas of drainage
- Lymphedema

Note: Isolated mild lymphadenopathy in the inguinal region used to be common in Indian subjects who used to walk bare footed, due to repeated trauma and infections of the lower limbs. With the improvement in socioeconomic condition, this situation has changed. In persons engaged in agricultural work with bare hands, the axillary nodes may be palpable. Enlargement of lymph nodes in other areas should raise suspicion of more serious disease.

Causes of Generalized Lymphadenopathy

Infections: Miliary tuberculosis, infectious mononucleosis, Human immunodeficiency virus (HIV) infection, German measles, filariasis secondary syphilis, trypanosomiasis (not present in India).

Other inflammatory disease: Systemic lupus erythematosus, rheumatoid disease, hypersensitivity reactions.

Neoplastic diseases: Lymphomas, acute leukemias, chronic lymphatic leukemia, blast crisis of chronic myelogenous leukemia.

Other conditions: Sarcoidosis, adverse reactions to drugs like dilantin sodium.

Localized Lymphadenopathy

Cervical Lymph Nodes

Enlargement of anterior cervical nodes, submandibular nodes and submental nodes may be due to primary lesions in the tonsils, mouth or teeth. Tuberculosis affects the anterior cervical groups

more often. Posterior cervical groups are affected in lesions of the scalp, secondary syphilis and leukemias. In lymphomas both anterior and posterior groups may be affected. Supraclavicular nodes are affected in pulmonary lesions such as malignancy. In african trypanosomiasis enlargement of posterior cervical nodes is characteristic ***(Winterbottom's sign)***.

The pretracheal nodes (scalene nodes, situated in between the scalene muscles and behind the sternal head of the sternocleidomastoid) are involved early in metastatic pulmonary carcinoma. In advanced malignancy of the esophagus the lower cervical nodes may be enlarged. Tuberculosis can present with isolated scalene node enlargement as well.

Axillary Nodes

These may be enlarged in infections of the upper extremities such as infected scabies. Ocassionally small axillary nodes may be seen in normal children and manual laborers. *In women neoplasms of the breast have to be particularly looked for.* Lymphomas, filariasis (especially *B. malayi*) and tuberculosis may involve the axillary nodes.

Epitrochlear (Supratrochlear) Nodes

These are enlarged secondary to sepsis in the hands and forearm. They may be enlarged in non-Hodgkin's Lymphoma, secondary syphilis and acute leukemias. Tuberculosis can present with enlargement of any lymph nodes.

Mediastinal Nodes

These are enlarged in lymphomas, acute lymphatic leukemia (T-cell type), secondary deposits from pulmonary neoplasms and in extensive metastases from abdominal and testicular tumors. Tuberculosis and sarcoidosis can present with mediastinal lymphadenopathy and constitutional symptoms especially in primary tuberculosis.

Abdominal Lymph Nodes

Regional groups are enlarged as a result of metastases from the areas of drainage. For example, pyloric nodes and nodes in the porta hepatis maybe secondary to gastric carcinoma or tumors of the hepatobiliary tract. Para-aortic nodes may be secondary to testicular or abdominal tumors. Mesenteric nodes may be secondary to neoplasms of the intestines, iliac nodes and pelvic nodes may be secondary to lesions of the cecum, ileocecal region, pelvic organs and prostate. Massive lymphadenopathy may occur in lymphomas and secondary malignancy.

Tuberculosis affecting the mesenteric nodes produce mild to moderate lymphadenopathy.

Inguinal Nodes

Characteristically inguinal adenopathy is seen in syphilitic chancre over the penis, lymphogra-nuloma venereum, filariasis, other infective and malignant lesions of the penis and vulva, melanoma in the feet and bubonic plague (rare).

Size of the Nodes

In systemic illness such as secondary syphilis, German measles, infectious mononucleosis and AIDS the size is small or only moderate (1–2 cm). Large sizes are attained in lymphomas, metastatic malignancy, lymphogranuloma venereum and diphtheria. Presence of large nodes in the upper part of the neck in faucial diphtheria gives rise to "bull neck" appearance. This is seen only rarely at present.

Number of Nodes

Enlargement may be confined to a single node or only a group in localized disease and in early stages of systemic diseases. Increase in the number of nodes and involvement of different groups signifies extension.

Consistency

Normal consistency (soft to firm) occurs in inflammatory diseases. When abscess formation or tuberculous caseation occurs, the nodes become soft or fluctuant. In lymphomas and chronic lymphatic leukemia the nodes are firm and rubbery. In primary syphilis the nodes are hard and discrete (shotty) and can be rolled under the skin. In metastatic carcinoma the nodes are firm to hard.

Tenderness

Pain on palpation and spontaneous pain are suggestive of inflammatory lesion. Lymphomas and metastatic lesions are nontender and painless.

Matting

In many cases the pathological process is confined to the node of affection without extending outside the capsule, e.g. lymphomas, syphilis, infectious mononucleosis. If the lesion ruptures the capsule and spreads to adjacent nodes and tissues, it leads to matting, i.e. the individual nodes cannot be identified separately. Two or more nodes appear to be sticking to each other. Sometimes the whole group is felt as a confluent mass, e.g. tuberculosis, metastatic carcinoma.

Lesions in the Area of Drainage

In many instances presence of an enlarged lymph node may be the first sign of disease in its area of drainage.

Examples

Axillary lymph node in the cancer of the breast Virchow's gland in cancer stomach. Cervical node in nasopharyngeal carcinoma. Bull neck in faucial diphtheria in a child. Inguinal nodes in melanoma of the foot. The importance of examining the area of drainage of the node should be borne in mind.

Lymphedema

Obstruction to lymph drainage results in retention of lymph in the interstitial spaces and lymphedema distally. Lymphedema is seen in conditions such as filariasis, metastatic deposits in lymph node and excision or irradiation of the nodes. Conditions such as tuberculous adenitis and lymphomas are not generally associated with lymphedema.

Lymph Node Fine Needle Aspiration Cytology (FNAC) and Biopsy

These are very common diagnostic procedures employed for diagnosing lymphatic disorders and systemic diseases. Being simple, safe and highly specific this procedure is resorted to in a wide variety of diseases.

Fine needle aspiration cytology (FNAC): Aspiration using a fine needle and examination of the material by cytology and histopathology is diagnostic in many cases. The material can also be used for microbiological tests. This has become a very common office procedure at present. If lymphoma is suspected and only one node is available it is better to do excision biopsy because needle aspiration might distort the hisotology.

Choice of lymph node for biopsy: In localized lymphadenopathy, the maximally affected node should be chosen. In gerneralized lymphadenopathy a node which shows moderate enlargement should be chosen. The smallest node may not show the typical lesion, whereas the largest one may show secondary changes such as necrosis which may alter the original histology. Axillary and inguinal nodes are not preferred for biopsy if other nodes are available.

Open biopsy: This is removal of the node or group of nodes for histopathology, touch preparations for cytology and microbiological tests. Open biopsy is done as a minor surgical procedure. This is indicated when the results of FNAC are equivocal and in conditions such as lymphoma where examination of the full node is helpful for complete diagnosis and to plan therapy.

Lymphangiography: This is the imaging procedure which delineates lymphatics and lymph nodes. This is done to visualize deep seated nodes such as iliac, para-aortic, retroperitoneal and mediastinal groups, but is seldom done now a days due to availability of other simpler imaging techniques.

Ultrasonography: This helps to identify the presence of enlarged nodes in the abdomen and pelvis, if the enlargement is moderate (above 0.3 cm in diameter) or severe. The nature of lesion can also be identified in many cases.

Smaller lymph nodes and deep seated lymph node groups can be better demonstrated by computed tomography and/or magnetic resonance imaging.

CHAPTER

3 Imagiology Studies

T Kesavan

Plain X-ray, Computed radiography, Digital radiography, Contrast studies, Digital subtraction angiography, Ultrasonography, Computed tomography, Magnetic resonance imaging, Nuclear imaging, Single photon emission tomography, Positron emission tomography

INTRODUCTION

Radiology, the art and science of imaging, has developed technically and technologically since the discovery of X-rays in the last part of 19th century. Though the basic concepts remain the same, refinement in all aspects of imaging and addition of newer techniques have widened the scope from purely diagnostic to interventional radiology. The specialty of radiology and imaging has application in all the branches of medicine.

German physicist Dr Wilhelm Conrad Roentgen (Fig. 3.1) discovered mysterious electromagnetic radiations of short wavelength which have the unique property of penetrating matter on 8th November 1896. He was experimenting with cathode ray tubes and as he was not able to find out the exact origin of the mysterious rays, he called them 'X-rays'. X-rays are electromagnetic radiations of very short wave length and are produced when fast moving electrons from a heated and negatively charged cathode hit a positively charged, high melting point anode, usually made of tungsten. The cathode and anode are enclosed in a completely evacuated glass tube. The energy of the electrons is converted to heat and X-rays. Only about 2% of the energy is converted to X-rays and the rest is converted to heat. The heat is removed from the anode by various methods of dissipation. Various modalities of imaging are aimed at visualizing the internal structure of the human body. Imaging can be either in the static mode or in the dynamic mode depending upon the clinical need and type of imaging modality. Modern imaging techniques can reveal considerable details of anatomy and pathophysiology of the various organs of the human body. Various types of contrast media can be introduced through oral, rectal, intravenous or intra-arterial route to facilitate visualization of the organs and tissues. The various

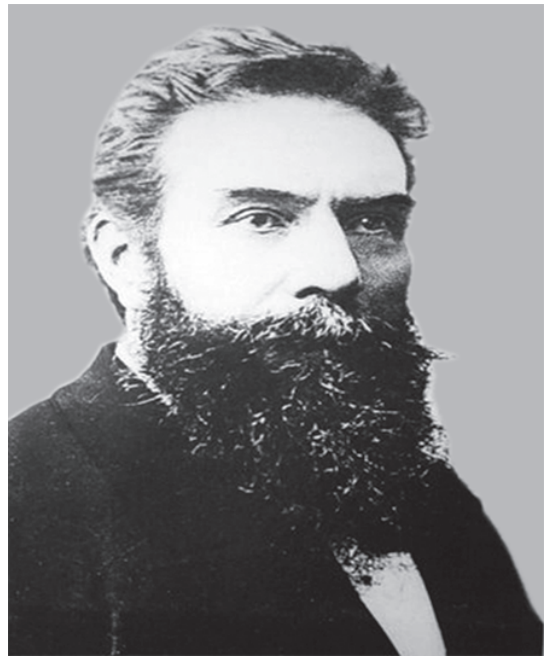


Fig. 3.1: WC Roentgen (1845-1923)
German physicist who discovered X-rays in 1896 and was awarded the first ever Nobel prize in 1901

methods to produce diagnostic imgages include plain X-rays, contrast studies and computed tomography (CT).

Plain X-Ray

X-rays penetrate tissues and are absorbed differentially depending on the basic elements contained in the tissues. Elements with low atomic number absorb little radiation (e.g. air, gas) and those with high atomic number absorb more (e.g. bones). The degree of absorption by fat and soft tissues comes in between. The attenuated X-rays coming out of the body are captured as an image on a photographic plate. The densities cast on the film vary from the extreme black produced by air or gas to extreme white cast by bones. Fat and soft tissues cast densities in between these two, the fatty tissue being less black than air. Thus, radiographically, we recognize four basic densities, namely air, fat, fluid and bone. A radiographic image is a depiction of these densities. The body part to be radiographed is interposed between the X-ray source and an image capturing device which traditionally is a photographic plate enclosed in a light tight box called the cassette. A pair of intensifying screens in the cassette converts the X-rays into visible light which exposes the film enclosed between them. The intensifying screens are coated with chemical substances called phosphors which emit visible light when X-rays fall on them. The emitted light may be blue or green depending on the phosphor, and the films used also are blue or green sensitive. This conversion from X-rays to visible light is important because the X-ray dose needed to produce a satisfactory image can be substantially reduced. The latent image formed on the photographic plate is processed in the dark room to get a radiograph. Now automatic processors are available which can process and dry the films within 60 to 90 seconds.

Computed Radiography

Computed radiography (CR) systems, convert the conventional analogue image to a digital format. The image capture is by means of an imaging plate (IP) made of photostimulable phosphor. The IP is enclosed in a cassette and is exposed as in conventional method. The IP, carrying the information is read by an image reader which uses a laser beam to convert the information on the IP into a digital image. After reading, the IP is erased by the same reader and is ready for reuse. The IP needs replacement after an average of about 50,000 to 60,000 exposures. The image is displayed on a monitor within seconds and can be manipulated, edited and printed. The image can be converted into hard copy using a laser camera or directly uploaded into a picture archiving and communication system (PACS). The advantages of CR are clarity of pictures, elimination of the dark room with environment unfriendly chemicals, long-term cost saving due to lesser spending on film, available X-ray equipment can be used, space saving because of storage and retrieval using CD/DVD, integration with PAC System for remote viewing and is a cheaper alternative to fully digital systems, which are at present prohibitively expensive. The main disadvantages are the very expensive imaging plates and slightly lesser degree of spatial resolution.

Digital Radiography

A flat panel detector usually made of amorphous silicon directly converts X-ray energy into digital signals to produce an image. As a result, there is substantial reduction in the X-ray dose required as compared to other systems. The detector panels are very expensive, heavy and fragile which, as on today, make their wide spread use restricted. However, digital radiography (DR) gives excellent spatial resolution and the images can be manipulated at a workstation. Integration with PACS is more efficient. The image display is immediate as in a digital camera. Currently, digital systems are available for conventional imaging including mammography.

CONTRAST STUDIES

These imaging procedures involve introduction of contrast media to enhance the image of a particular body region or structure. The contrast may be negative (e.g. air, CO_2) or positive (e.g. barium or iodinated contrast media). Negative contrast media produce black densities and positive contrast media produce white densities compared to body tissues. Contrast studies can be used to delineate the GI tract, urinary tract, venous and arterial system and brain and the spinal cord.

GI Tract

Upper and lower GI tracts can be studied using a fine suspension of barium sulphate. Barium sulphate is a nonabsorbable, inert, heavy metal salt which coats the mucosal surface of the GI tract so that various lesions like growths, ulcers, or congenital anomalies can be easily diagnosed. Barium swallow is done to evaluate the esophagus and barium meal to study the stomach and duodenum up to the duodeno-jejunal flexure (Figs 3.2 and 3.3). Commercially available gas producing mixtures can be used to do double contrast studies of the upper GI tract to delineate mucosal lesions better. Barium meal follow through studies are intended to evaluate the small bowel up to the ileocecal junction.

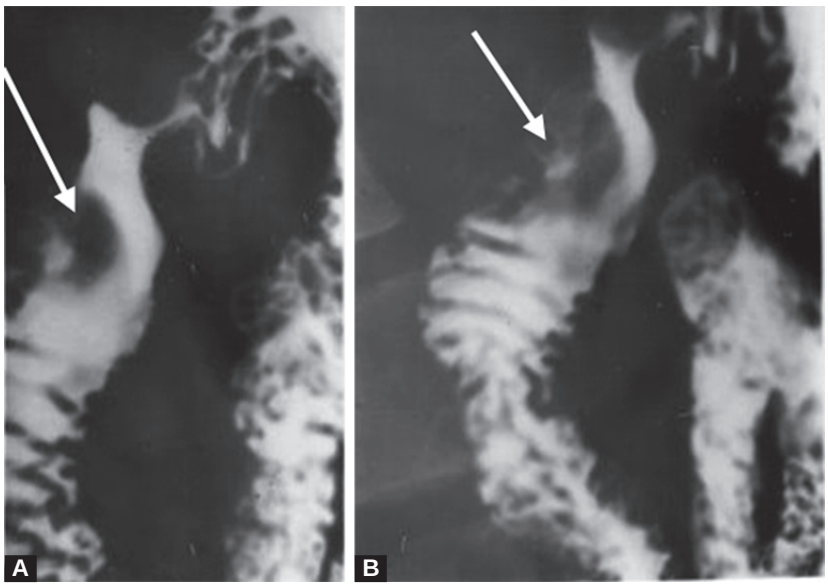
For a good barium enema study, the colon need to be prepared thoroughly with low residue diet, purgatives, soap and water enema and bowel wash. Barium enema involves study of the large bowel after introducing barium suspension through the rectum. In double contrast enema, air or carbon dioxide can be introduced after partial evacuation of the barium to get distension of the bowel which makes diagnosis of mucosal lesions extremely simple and effective.

Urinary Tract

The imaging of the urinary tract is done either by giving water soluble iodinated contrast media intravenously or by introducing such contrast through the urethra into the bladder using a catheter.



Fig. 3.2: Double contrast barium meal showing normal stomach and deformed duodenal cap (arrow)



Figs 3.3A and B: Spot film of duodenal cap of the same case showing active ulcer crater with marked edema around the ulcer (arrows)

The former procedure is called intravenous urography/pyelography (IVU/IVP) and the latter is known as micturating cysto-urethrography (MCU). The contrast media are tri-iodinated compounds produced by substituting three hydrogen atoms of an organic molecule with iodine, the organic molecule being basically the benzene ring. [127] Iodine is responsible for the opacification and is found to be the most satisfactory element to be introduced into sensitive organs like the kidneys, heart and brain. Contrast media available earlier had their molecules in the solution in an ionized form. But the currently available contrast media are nonionic, that is the anions and cations do not dissociate in the solution. The ionic media caused more reactions than the newer nonionic media, which are better tolerated by the patients after administration. After IV injection, the contrast is removed from the blood by glomerular filtration. It is not reabsorbed but made more concentrated due to the reabsorption of water in the renal tubules. Sequential films are done to delineate the anatomy of the urinary tract while it is opacified by the contrast containing urine. As excretion of contrast and its concentration depend upon good glomerular filtration and water reabsorption, IVU is also a measure of renal function. IVU can be employed in the diagnosis of renal calculi, trauma, and neoplastic and inflammatory lesions of the urinary tract. Micturating cysto-urethrography (MCU) is done by introducing dilute water-soluble contrast into the bladder using a catheter which is removed immediately. Exposures are made during voiding to assess the lower urinary tract dynamically. MCU is used to diagnose vesico-ureteric reflux, bladder outlet obstruction (congenital or traumatic) neurogenic bladder, study the posterior urethra and look for posterior urethral valve (Fig. 3.4).

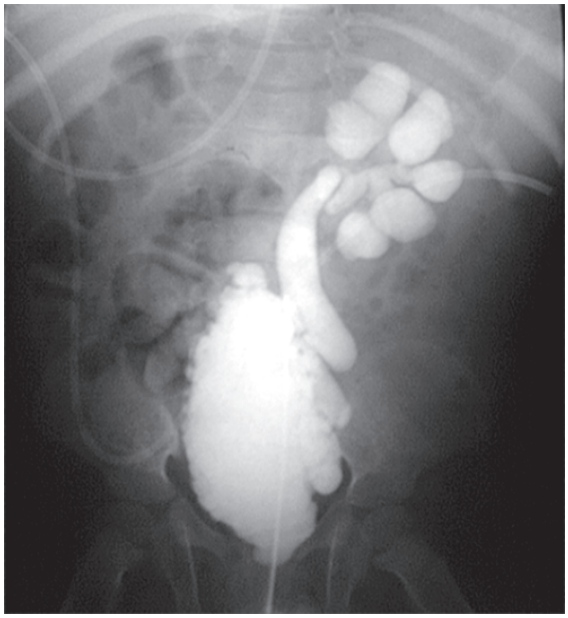


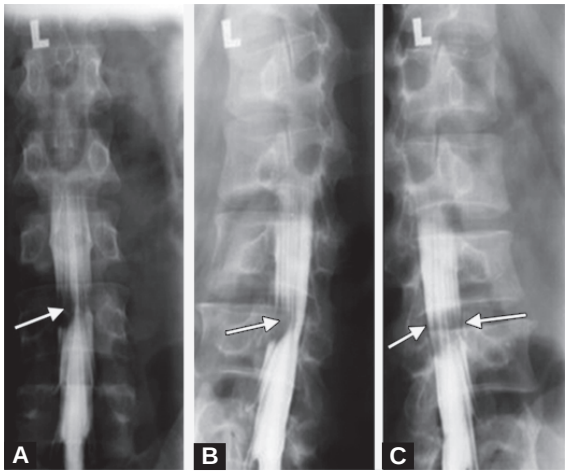
Fig. 3.4: Micturating cystourethrogram showing large trabeculated bladder with unilateral dilated ureter and pelvicalyceal system when dye is introduced by catheter. Reflux is noted even during the bladder filling phase

Myelography

This is done to visualize the subarachnoid space along with spinal cord. Myelography is performed by injecting contrast into the subarachnoid space through a lumbar puncture (Figs 3.5A to C) or rarely a lateral cervical puncture. The oily contrast materials used earlier have been completely replaced by safer water soluble nonionic media because of lesser complications rate. They remain in the system for less than 12 to 16 hours and cause less serious complications like headache, back pain, radicular pain or rarely arachnoiditis. The total amount of contrast must not exceed 3 g of iodinated dye. With the advent of MRI, this invasive procedure has been abandoned.

Angiography

Water soluble contrast is injected into an artery through a catheter which is positioned into the artery under fluoroscopic control to the desired position. Contrast is injected either by hand or by a pressure injector. These days, arteriography for



Figs 3.5A to C: Myelography using water soluble contrast showing large bilateral lateral intervertebral disk prolapse at L3/4 (arrows)

diagnostic purposes is often combined with therapeutic maneuvers since most of the information obtained by angiography can be obtained by less invasive procedures like ultrasonography, CT and MRI.

Digital Subtraction Angiography

Digital subtraction angiography (DSA) is made possible due to the ability of modern angiography machines to acquire data digitally which facilitates easy storage, processing and retrieval. It is also possible to make masks before injection of contrast so that the masks can be subtracted from the contrast image to get rid of dense bony parts like the skull, spine, etc. The digitally acquired image can be manipulated using post-processing algorithms. The DSA is indispensable to the interventional radiologist as catheter advancing and positioning can be observed real time and display of the angiographic images are instantaneous and can be reviewed immediately. The acquired images can be analyzed both qualitatively and quantitatively later. Like other digitally acquired images, these also can be uploaded into a PAC System for remote viewing and analysis (Fig. 3.6).

Complications of Angiography and Adverse Reactions to Intravascular Contrast Media

Intravascular contrast agents can potentially produce adverse reactions ranging from mild nausea, vomiting and urticaria to severe laryngeal edema, cardiac arrest or even death. Currently used nonionic agents have remarkably reduced incidence of adverse effects. These reactions are not anaphylactic but are termed anaphylactoid as the severity of adverse reaction is not dose related as is the case in anaphylactic reactions. Hence every precaution to prevent and/or treat such adverse events should be taken whenever intravascular contrast agents are used. Complications peculiar to arteriography are in addition to those relating to contrast agents. Some of the common complications are directly related to arterial puncture and introduction of the catheter. They are local hematoma, local sepsis, dissection, thrombosis of the artery, pseudoaneurysms, AV fistula, etc.

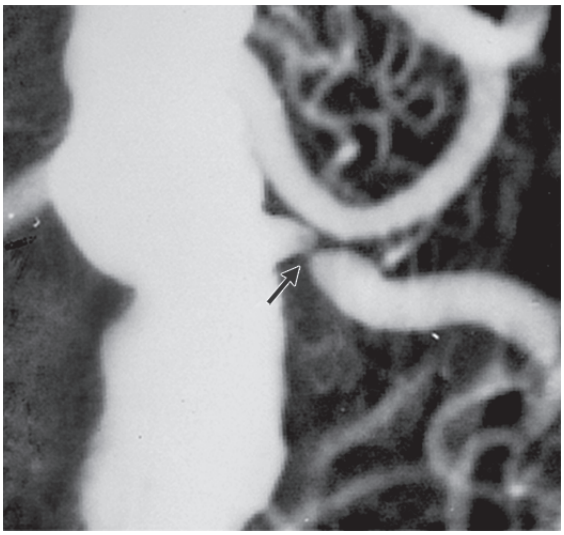


Fig. 3.6: Digital subtraction flush abdominal aortogram showing irregularly dilated aorta and narrowing of left renal artery shortly after its origin (arrow)

ULTRASONOGRAPHY

Ultrasonography scan (USS) is the imaging technique for soft tissues using high frequency sound waves far above the audible frequencies of the human ear. The usual frequencies employed in diagnostic imaging are from 1.5 MHz to about 20 MHz. Ultrasonography in medicine came into being immediately after World War II and is a direct extension of the SONAR (sound navigation and ranging) which was widely used in the war for submarine navigation. The transducers of the ultrasound machine produce high frequency sound waves by making use of an array of piezoelectric crystals usually made of the ceramic, lead zirconate titanate (PZT). These crystals also act as receivers of the reflected sound waves which are converted to electrical signals. These in turn are translated into a gray scale image by the computer and displayed on a monitor. Sound waves propagate in the tissues and are reflected back at tissue interfaces. As the frame rate of reproducing the images are quite fast, the images are real time. This is the most important advantage of ultrasound imaging. The gray scale image is called a B mode image as it is composed of thousands of brightness spots. Ultrasound can also depict rhythmic movements like that of the heart and its valves. This mode is called the M mode or motion mode. In Doppler mode, it can also be used to study arteries and veins on the principle of Doppler effect which is defined as a change in the perceived frequency of sound emitted by a moving source. Doppler can evaluate arteries and veins in

color and can also measure velocities of flowing blood. Hence Doppler is an excellent method to diagnose various lesions of the arteries and veins like stenosis, aneurysms, thrombosis, etc. Transducers with various frequencies are used depending upon the tissue to be imaged. Lower frequencies are used to visualize deeper tissues and higher frequencies for more superficial structures as penetrability is inversely proportional to the frequency. Thus, to scan the abdomen, a 2 to 5 MHz transducer is used and to visualize the thyroid, a frequency range of 10 to 12 MHz is appropriate. Usually the images obtained with an ultrasound machine is called a 2D image. Now special transducers which can produce 3D images are also available. Ultrasound has the advantage of being noninvasive, comparatively cheap, easily reproducible and without the hazard of ionizing radiations with no known ill effects or discomfort to the patient. However, ultrasonography is highly operator dependent and the results are directly proportional to the experience and expertise of the operator. Ultrasound cannot propagate through air or gas and also bone and hence is unsuitable to examine air containing organs like the intestine and lungs and structures enclosed within bony structure like the brain and spinal cord. The only exception to this is the infant brain which can be evaluated through the open fontanelle. Recently, ultrasonic contrast media containing micro bubbles have been introduced which can be used to evaluate tumors and tumor like lesions of the liver, breast and thyroid.

COMPUTED TOMOGRAPHY

Computed tomography (CT) was invented by Sir Godfrey Hounsfield and was first used in 1972. First CT scanners could only be used to scan the brain as scan times were prolonged and could not scan moving structures. The basic principle of CT is that the internal structure of an object can be reconstructed from multiple projections of the object. The energy used in CT is X-ray. Thin beam of X-ray is passed through the body from various angles of 180 to 360 and the emerging X-ray photons are picked up by an array of detectors. The signals from the detectors are processed by a powerful computer to reconstruct the image using mathematical algorithms into slices of desired thickness. The reconstructed images are displayed on a monitor. CT scanners have three basic components:

1. The gantry which houses the X-ray source, detectors and high voltage generators.
2. A patient couch to 'feed' the patient into the gantry.
3. Computer system with monitors for processing and display of images.

Figures 3.7 and 3.8 show normal CT brain and CT abdomen.

Over the past almost four decades, CT technology has advanced exceptionally both in the

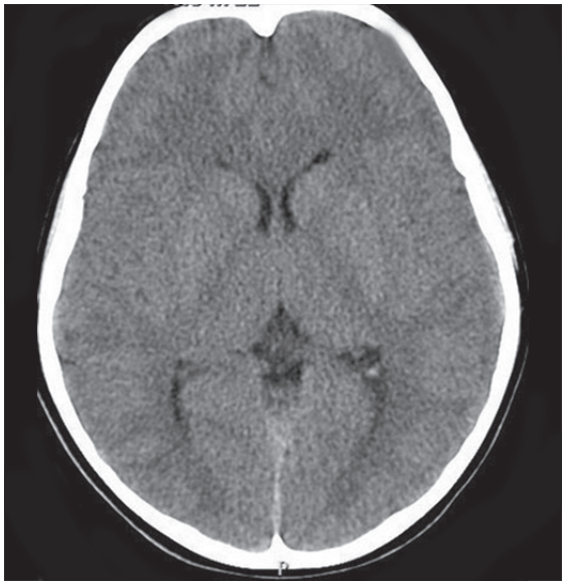


Fig. 3.7: Normal brain CT—without contrast

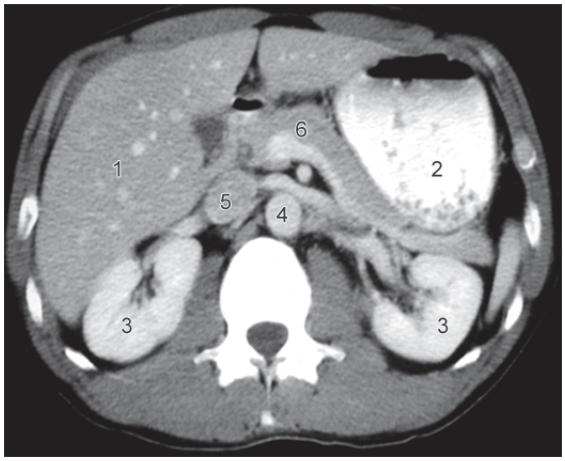


Fig. 3.8: CT abdomen with oral and IV contrast. Liver, stomach, kidneys, aorta, inferior vena cava and pancreas are seen in this picture (serially numbered 1–6)

development of high capacity X-ray tubes and tremendous computer power such that the scanners have become extremely fast with scan times as low as 250 milliseconds as compared to the scan times of the original scanners which took more than 5 minutes for one slice. Instead of sequential single slices obtained by earlier scanners, helical scanning with multiple row of detectors has made acquisition of a volume of tissue in thin slices, as thin as 0.25 mm possible so that exquisite 3D images of any organ can be reconstructed. CT can be used in a variety of clinical conditions, ranging from trauma, inflammatory and neoplastic conditions to noninvasive coronary imaging.

With the advancement of spiral or helical CT, there are no areas of the human body, which cannot be imaged using this technology. Helical scanning with very fast acquisition times and advanced detector designs have made 2D and 3D reconstructions and CT angiography (CTA) extremely simple and effective. Reconstructed 3D images can be rotated in any desired direction for viewing and analysis. Softwares are available for making various measurements like percentage of stenosis, length of stenotic segment, etc. Straightening out tortuous portions of an artery, like coronary vessels, can also be done with virtual vascular endoscopy. (Figs 3.9 to 3.11)

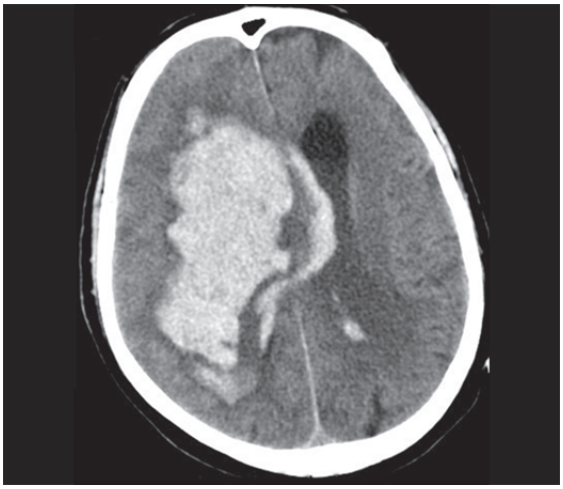


Fig. 3.9: CT brain showing intracranial hemorrhage with intraventricular extension

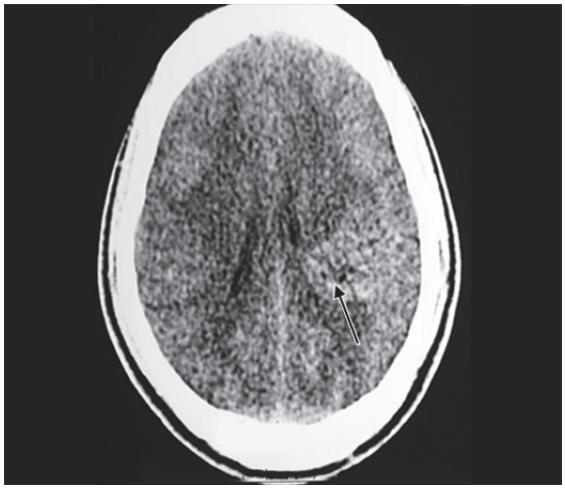


Fig. 3.11A: Plain CT showing ill-defined hyperdense lesion in the left posterior parietal area (arrow)

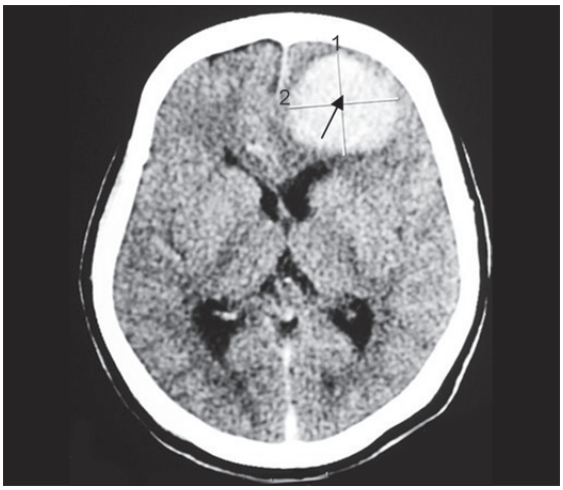


Fig. 3.10: Frontal meningioma. Contrast CT brain showing marked enhancement of the tumor (arrow)

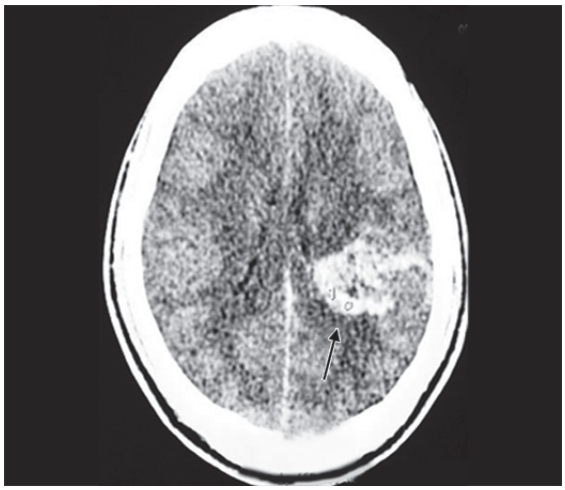


Fig. 3.11B: Postcontrast CT of the same case showing serpiginous vascular channels in the posterior parietal area typical of arteriovenous malformation (arrow)

CT Angiography

CT angiography (CTA) is a noninvasive procedure which can be used to study the arteries and veins of any part of the body. Usually about 100 ml of water soluble contrast is injected intravenously at a high rate (2–5 ml/sec) using a pressure injector and images can be acquired in the arterial and venous phases. The exposures can be triggered automatically by programming the machine when the contrast reaches a particular concentration in the desired artery (Figs 3.12 to 3.14).

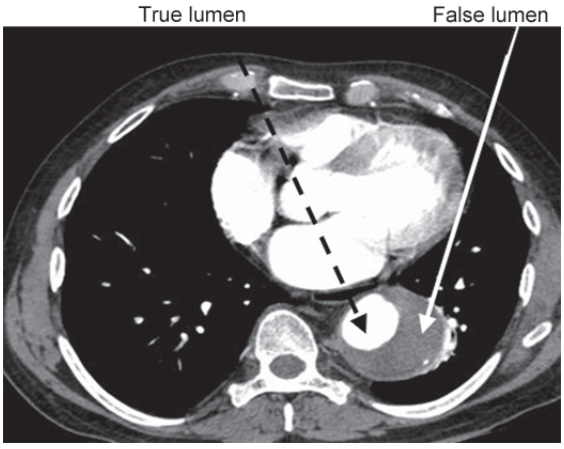


Fig. 3.12: CT angiogram, axial section showing extensive dissection of the aorta. Note the true lumen (black arrow) filled with contrast and also the false lumen which is eccentric and thrombosed (white arrow)

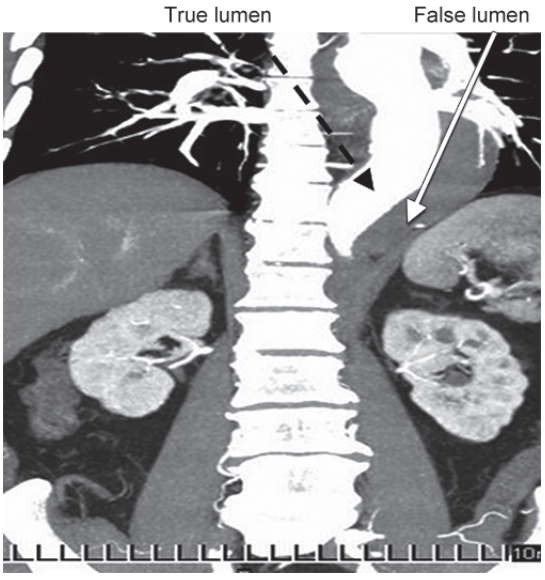


Fig. 3.13: Coronal reconstruction of the same case showing the dissection of aorta in the descending thoracic and upper abdominal segments

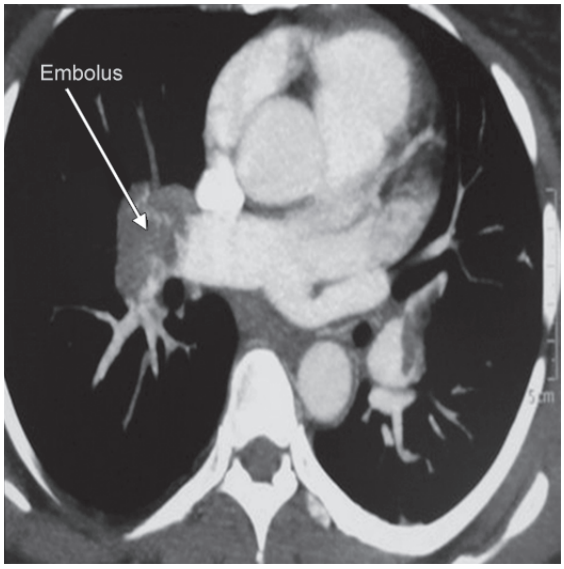


Fig. 3.14: CT pulmonary angiogram showing large filling defect in the pulmonary artery (arrow) in a case of pulmonary embolism secondary to deep vein thrombosis of lower limbs

Automatic injectors can be programmed to inject the contrast at the desired rate and time frame with facilities to include a time delay if required. Special studies like brain perfusion are possible to evaluate any compromise in the vascular supply to a particular territory in cases of stroke before CT signs of infarction set in, so that thrombolytic therapy can be instituted to salvage the affected part of the brain before permanent damage occurs. Multidetector CT (MDCT), which can acquire 320 slices per rotation of the gantry are now available which can render the images so fast that a contrast study of the brain virtually appears real time with the arterial, capillary and venous phases being displayed in very quick succession. The coverage is so large and acquisition so fast that the entire brain can be studied with one gantry rotation and the coronary arteries in just one or two cardiac cycles.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) is a medical imaging technique to visualize detailed internal structure of the body. It produces better soft tissue differentiation than CT and can be used in the imaging of the nervous system, musculoskeletal system, cardiovascular system and also in oncology. Unlike CT, it does not use no ionizing radiation and

as far as is understood has no ill effects on the human body. Now let us try to understand the term MRI.

The Magnet (M)

This is the most important component of the equipment and its strength is measured in Tesla. The machines in use at present have field strengths of 0.2 to 9 tesla. The basic unit of magnetism is Gauss (1 tesla =10,000 gauss). The earth's magnetic field is 0.5 gauss. So it is evident how powerful the magnets are. There are different types of magnets like permanent magnets, resistive magnets and superconductor magnets. Permanent magnets are very heavy and large hence only smaller field strengths are practical. Resistive magnets need constant supply of large current without interruption and not commonly used. Today, large field strength magnets are superconductors. Superconductivity is a phenomenon in which there is zero resistance to the flow of current when certain materials are cooled to near absolute zero (about 4 K). This means that when an electric current is passed through the material to achieve the desired magnetic strength, the current will continue to flow even when the external power supply is turned off. The extreme cooling is achieved by immersing the magnet in liquid helium in an evacuated stainless steel container.

Resonance (R)

Nuclei of certain atoms like hydrogen when placed in a strong magnetic field absorb and emit energy of a specific frequency. Hydrogen atoms have a single proton in their nuclei and so possess a net charge and angular movement. Hydrogen atoms are abundant in the body and behave like freely suspended small bar magnets spinning rapidly about their magnetic axes. Other atoms which have the same property are sodium, phosphorus, carbon, etc. Rare gases like helium and xenon can be made sensitive to the same phenomenon and can be used in the study of the airways and for blood perfusion respectively. The hydrogen nuclei when placed in an external magnetic field align themselves in the direction of the magnetic field and continue to rotate in the same frequency about the magnetic field. This is called "precession". The frequency is directly proportional to the external magnetic field and is called the Larmor frequency. When an oscillating pulse of a matching radio frequency is applied on the group of protons, there is a strong interaction or resonance. This phenomenon is called magnetic resonance. In the interaction, energy is absorbed by the protons causing a change in direction of their magnetic field. The angle of deviation of the magnetic field depends on the strength and duration of the pulse. Usually 90 degree and 180 degree pulses are used. When the signal is turned off, the nuclei come back to their original equilibrium and in the process release energy. This induces a small voltage in a receiver coil kept near the patient. This signal is called the free induction decay (FID). The magnitude and length of the signal is determined by the nuclear relaxation times. First of these relaxation times is T1 which is the longitudinal relaxation time and is the time taken by nuclei to return to thermal equilibrium. T2 is transverse relaxation time, that is the characteristic time of FID. T1 and T2 are important determinants of tissue contrast. The pulse has two selectable times which are called TR and TE. TR is the time interval between two 90 degree pulses or Time Repetition. TE is the time interval between the middle of a 90 degree pulse and the middle of a 180 degree pulse. Typical TR intervals are between 500 to 3000 ms and TE intervals range from 30 to 150 ms. When a short TR and short TE are used a T1 weighted image is obtained and a long TR and long TE results in a T2 weighted image. Various tissues in the body have different relaxation times. For example, T1 of brain tissue is short and that of CSF is long. So in a T1 weighted sequence, the brain will appear bright but the CSF will appear dark as its T1 is long. This means that brain will give a signal earlier than CSF in T1. The reverse is true with T2. Here CSF will appear bright and the brain will appear dark. Once the signals are collected by the rf coils, these are processed by the computer in a complex mathematical analysis called Fourier analysis and the transformation of the signals to the visual image is called Fourier transformation. Slices of desired thickness are obtained by selective excitation by the application of a gradient field during the rf pulse so as to isolate the plane of interest. The main magnetic field opposes the gradient field and the noise that is heard in the MR machine is due to this. The higher the field strength of the main magnet, the more will be the noise which

can reach as high as 85 dBS. Patients need to be offered ear plugs to reduce the discomfort. Other imaging techniques using MR are MR angiography, MR spectroscopy, functional MRI, etc. Paramagnetic substances like chelates of gadolinium are injected intravenously and these substances alter the signal intensities by reducing the T1 and T2 relaxation times to varying extents in various tissues.

Safety and Hazards

MRI produces no ill effects on the body. But remaining still for considerable period of time inside the closed tunnel like gantry with all the noise cannot be tolerated by many who are claustrophobic. Magnetic substances like pacemakers, orthopedic devices like plates and joint implants, aneurysms clips, etc. are absolute contraindication for doing MRI as these can act as dangerous missiles in the high magnetic field. The MR contrast media are now known to cause irreversible and progressive fibrosis of the skin, joints and the eye in patients who are in renal failure. This entity is known as NSF (Nephrogenic systemic fibrosis).

CT vs MRI

The usual question asked is whether MRI will replace CT. The answer is "no". Because they are only complementary to each other. CT is indicated in acute traumatic cases, such as head injury since it can demonstrate acute hemorrhage well whereas MRI cannot, since the MRI depends on degraded hemoglobin to produce the image. It is insensitive to fresh hemoglobin. MRI can show soft tissue details exquisitely whereas CT is less efficient. Calcifications cannot be detected by MRI, but CT can pick up even subtle calcifications.

NUCLEAR IMAGING

This is a medical imaging technique using ionizing radiations emitted by particular radiopharmaceuticals when introduced into the body. Radionuclides are unstable isotopes of several elements. When their decay occurs, they release energy as electromagnetic radiation called gamma radiation. The emitted radiation is detected by a gamma camera which has a scintillating crystal such as sodium iodide which emits visible light when radiation falls on it. This light is amplified and reconstructed to produce an image. Commonly used radiopharmaceuticals contain ^{99m} technetium which is tagged with various molecules to make them organ specific. Other radionuclides include ^{123}iodine, and ^{131}iodine, ^{11}carbon, ^{13}nitrogen, ^{15}oxygen, ^{18} fluorine, etc. There are two types of imaging in nuclear medicine, they are SPECT and PET.

Single Photon Emission Computed Tomography

Single photon emission computed tomography (SPECT) involves detection of gamma rays singly from a radionuclide like ^{99m} technetium or ^{201} thallium to produce a tomographic image.

Positron Emission Tomography

These equipments are designed to detect paired photons which are 180 degrees apart emitted by the annihilating positron. There is a ring of detectors made of bismuth germinate. These are designed to detect gamma rays of 511keV (kilo electron volts). These signals are used to construct 2D and 3D images of the organ being imaged. The radionuclides used in positron emission tomography (PET) scanners are ^{11} carbon, ^{15} oxygen, and ^{18} fluorine. PET has more sensitivity and spatial resolution than SPECT. The PET can be used to analyze the metabolic activity of tumors by using ^{18} fluorine labeled deoxyglucose (FDG).

Indications for Nuclear Imaging

Some of the common indications for nuclear imaging are:

1. Myocardial perfusion
2. Blood flow distribution of brain tumors
3. Hepatobiliary imaging
4. Renal function
5. Ventilation perfusion study of lungs
6. Thyroid nodule
7. Neuroendocrine tumors.

FURTHER READING

1. Christensen's Physics of Diagnostic Radiology. 4th edition—Thomas S Curry, James S Dawdey and Robert C Murray.
2. Diagnostic Ultrasound—Carol M Rumack, Stephanie R Wilson and J William Charboneau.
3. Grainger Allison's Diagnostic Radiology.
4. Textbook of Radiology and Medical Imaging—David Sutton.

SECTION

3

Alimentary System

CHAPTER

4 Alimentary System: General Considerations

KR Vinaya Kumar

Gut flora, Gastrointestinal hormones, Pattern of alimentary diseases

INTRODUCTION

Gastrointestinal system (GI) extends from mouth to the anus and comprises several organs with distinct functions. Upper gastrointestinal tract extends up to the ligament of Treitz (demarcates duodeno-jejunal flexure). GI tract serves two main functions—assimilation of nutrients and elimination of waste.

Swallowing is initiated as a voluntary process, by concerted muscle action involving the lips, cheeks, tongue, and pharyngeal muscles. Once the food passes down the oropharynx, swallowing becomes a reflex act. The esophagus which is 25 cm long transmits food into the stomach by active peristalsis.

Gastric contents are prevented from regurgitating into the esophagus by the intrinsic sphincter at the lower end of esophagus, anatomical configuration of gastroesophageal junction and muscular action of diaphragm. The lower esophageal sphincter is a high pressure zone of about 20 mm Hg at rest. It is more physiologic and less well defined anatomically. The resting tone is maintained by circular smooth muscle fibers and gastric sling smooth muscles on the left.

Stomach acts as the reservoir of food. The food ingested during a meal remains in the stomach for 2 ½ to 3 hours. The process of digestion starts here. Peristaltic movements of the stomach help to send its semisolid contents through the pylorus into the duodenum, jejunum, and ileum for digestion and absorption. Distension of the stomach is visible as a swelling in the epigastrium. When the gastric outlet is obstructed, peristaltic waves become prominent. They move from the cardia towards the pylorus and in thin individuals these may be quite visible. Visible gastric peristalsis should suggest obstruction of gastric outlet. Ulceration of the mucosa of stomach or first part of duodenum is common and several factors such as invasion by *Helicobacter pylori*, increased acid production and impairment of the natural protective mechanisms of the mucosa by drugs play the major role.

The *small intestine* consisting of duodenum, jejunum and ileum, has a major role in digestion and absorption. Digestion proceeds with the help of bile, pancreatic juice and intestinal juices which provide the physicochemical environment and enzymes to digest the constituents of food.

The *common bile duct* and *pancreatic duct* join the second part of duodenum at the ampulla of Vater, which is a common site for obstruction by calculi and tumors. When the small intestine is obstructed, the distended loops are visible around the umbilicus as steps in a ladder (ladder pattern). Digested food which has undergone partial absorption enters the ileocecal valve which is situated in the right iliac fossa. The contents of the cecum are fluid. There is some delay for the onward passage of material from the cecum and this stasis predisposes to infections.

Therefore, cecum is a common site to be affected in amebic dysentery and tuberculosis. The transit

time for food from stomach to the cecum is 2.5 to 3.0 hours. The progress of a radiopaque contrast material can be followed up from the mouth to the anal canal by radiography (barium meal).

GUT FLORA

It is a complex microbial ecosystem, colonizing the gut wall, living together in harmony in the gut. In health, these microbes are prevented from entering the systemic circulation by natural mucosal and other defense mechanisms.

Colonization of GI tract of newborn infants starts immediately after birth and occurs within a few days.

The composition of gut flora varies from mouth to the colon. The intestinal mileu favors the growth and multiplication of several microbes, both aerobic and anaerobic. The milieu in the cecum and ascending colon favor the growth of carbohydrate splitting organisms. Towards the distal portion of large intestine, the flora change to protein splitting organisms. The main anaerobic genera include Bacteroide, Bifidobacterium, Eubacterium, *Peptococcus*, *Peptostreptococcus*, *Clostridium* and *Ruminococcus*. The aerobic flora include *Escherichia*, *Enterobacter*, *Enterococcus*, *Klebsiella*, *Lactobacillus*, and *Proteus*. Alterations in the gut flora and break down of the defense mechanisms and the mucosal barrier are the main factors in several diseases states such as diarrheal diseases, septicemia, multiorgan failure syndrome and others leading to hepatic encephalopathy and others.

Metabolic Activity of the Flora

1. Production of regulatory signals for mucosal and immune homeostasis
2. Bio-transformation of the bile acids
3. Breakdown of dietary oxalate
4. Conversion of pro-drugs to active metabolites
5. Degradation of polysaccharides of plant origin
6. Production of folate, B-complex vitamins, and vitamin K
7. Production of nutrient short chain fatty acids
8. Regulation of fat storage.

GASTROINTESTINAL HORMONES

Chemical transmitters of the gut are produced by discrete cells of the gastrointestinal mucosa. They are classified as endocrine, paracrine, synaptic (neurocrine) or autocrine. Specialized signaling cells that secrete transmitters into the blood are known as endocrine cells. The transmitters they produce are called *hormones* (Table 4.1).

Table 4.1: Peptide hormones of the gastrointestinal tract

1.	Gastrin
2.	Cholecystokinin
3.	Secretin
4.	Vasoactive intestinal polypeptide (VIP)
5.	Glucagon
6.	Glucose dependent insulinotropic polypeptide
7.	Pancreatic polypeptide
8.	Substance P and the tachykinins
9.	Somatostatin
10.	Motilin
11.	Leptin
12.	Ghrelin

PATTERN OF ALIMENTARY DISEASES

Esophageal diseases give rise to dysphagia and this is usually caused by carcinoma, stricture, ulceration, external pressure from mediastinal structures or neuromuscular incoordination. Esophageal varices developing in portal hypertension is a common cause for hematemesis. In the gastroduodenal region—gastritis, gastric and duodenal ulcers and carcinoma stomach top the list. The common small intestinal diseases include infective and noninfective diarrheas, malabsorption states, functional disorders like irritable bowel syndrome, obstructions and neoplasia. The ileocecal region and the cecum are common sites for intestinal tuberculosis, amoebiasis, inflammatory bowel disease and lymphoma. The appendix may get inflamed acutely, i.e. acute appendicitis which is a common surgical emergency. Large intestinal problems include constipation, diarrhea, infective colitis, inflammatory bowel disease, carcinoma, angiodysplasia, and diverticular disease. Hemorrhoids are among the most common disorders affecting the population at large.These are often unnoticed but they form an important source of blood loss.

The alimentary tract is a common site for neoplasms. In the order of frequency they are:

1. Oral cancer
2. Esophageal cancer
3. Gastric cancer
4. Hepatocellular carcinoma
5. Colon cancer.

In addition, alimentary tract is a common site for lymphomas, particularly ileocecum, stomach and rectum.

Changing Pattern of the Diseases

Esophageal cancers are becoming increasingly common now and are observed more in the lower end than in the middle third. Chronic calcific pancreatitis, pancreatic neoplasms and colonic neoplasms are on the increase. Ulcer disease due to *H. pylori* is increasingly being encountered. Reflux disease, irritable bowel syndrome and inflammatory bowel diseases are also increasing. Viral hepatitis is still an important problem. Cirrhosis and hepatocellular carcinomas are increasing. Widespread use of drugs such as aspirin, non-steroidal anti-inflammatory drugs (NSAIDs), statins, corticosteroids and others are causing gastrointestinal problems such as gastritis, bleedings and other GI emergencies. Diseases such as non-alcoholic fatty infiltration of the liver, alcohol related problems and others are also showing an increasing trend.

However, intestinal tuberculosis, amebic liver abscesses and tropical sprue are showing a decreasing trend.

CHAPTER

5 Symptoms in Alimentary Diseases

KR Vinaya Kumar

Dysphagia, Dyspepsia, Heartburn, Vomiting, Diarrhea, Constipation, Alteration of bowel habits, Flatulence, Gastrointestinal (GI) bleed, Hematemesis, Melena, Hematochezia, Bleeding per rectum (PR), Abdominal pain, Abdominal distension, Jaundice, Pruritus, Steatorrhea, Weight loss, Fever

The important symptoms in gastrointestinal diseases are given in Table 5.1.

Table 5.1: Important symptoms in GI diseases

Dysphagia
Dyspepsia
Heartburn
Vomiting
Diarrhea
Constipation
Alteration of bowel habits
Gastrointestinal (GI) bleed
Hematemesis, melena,
Hematochezia, bleeding per rectum (PR)
Abdominal pain, flatulence
Abdominal distension
Jaundice
Pruritus
Steatorrhea, weight loss, fever
Gastrointestinal (GI) bleed after flatulence

DYSPHAGIA

Definition

Dysphagia is the sensation of sticking or obstruction of passage of food through mouth, pharynx or esophagus. Most common serious cause of dysphagia is esophageal carcinoma. Now the most common site of esophageal cancer is the lower end. A good history can provide a probable diagnosis in approximately 80% of the patients. Since the act of swallowing involves coordinated sensory and motor actions of several structures like oropharynx and esophagus, dysphagia may result from several causes (Table 5.2).

Table 5.2: Common causes of dysphagia

Oropharyngeal dysphagia	*Esophageal dysphagia*
Structural Causes	**Motility Disorders**
Carcinomas	Achalasia
Zenker's diverticulum	Diffuse esophageal spasm
Webs	Nutcracker esophagus
Prior surgery/radiation	Spasm of lower esophageal sphincter
Infections of pharynx/neck	Ineffective esophageal motility
Thyromegaly	Scleroderma
Areal dysphagia	Reflux-related dysmotility
Neuromuscular causes	*Structural disorders*
Stroke	Tumors
Parkinson's disease	Peptic stricture
Myasthenia gravis	Lower esophageal (Schatzki) ring
Multiple sclerosis	Other esophageal rings and webs
Myopathies	Diverticula
CNS tumors	Medication induced strictures
Motor neuron diseases	Foreign bodies
	Extrinsic compression

Odynophagia denotes pain on swallowing. This can be due to pill esophagitis, infection with candida and cytomegalovirus, injuries by foreign bodies, burns and others.

Sitophobia: It refers to the fear of eating because of the subsequent abdominal discomfort usually seen in mesenteric ischemia.

Phagophobia: It is the fear of swallowing seen in hysteria, tetanus and rabies (mainly due to fear of aspiration).

Globus hystericus is the sensation of lump lodged in the throat. Often it is not associated with any physically demonstrable abnormalities. Many cases are associated with hysteria.

History of nasal regurgitation and aspiration favors pharyngeal paralysis or tracheo-esophageal fistula. Hoarseness of voice indicates recurrent laryngeal nerve involvement which may be due to carcinoma of bronchus. A carcinoma usually presents as dysphagia to solids first, later on to liquids as well. It is accompanied by weight loss and is rapidly progressing. Benign esophageal strictures or functional obstruction such as esophageal spasm and motility disorders present with same picture, but the progression is slow.

Neurogenic dysphagia: This manifests as dysphagia mainly to liquids. Other neurological symptoms help to localize the lesion. In unilateral paralysis of 9th and 10th cranial nerves, the coordinated mechanism for swallowing becomes defective and therefore fluids which require fast action for swallowing regurgitate through the nose, where as solids can still be swallowed with difficulty.

Achalasia cardia is a rare cause of dysphagia where there is failure of relaxation of lower esophageal sphincter (LES). Diffuse esophageal spasm presents as chest pain with dysphagia.

Plummer-Vinson (Patterson Kelly) syndrome: In this syndrome, dysphagia felt as a painful obstruction at the postcricoid level of the pharynx generally associated with iron deficiency states. In many cases it is reversible with treatment.

DYSPEPSIA

Dyspepsia is the persistent pain or discomfort centered in the upper abdomen of more than three months duration. This is one of the common symptoms in gastroenterology. Dyspepsia may be caused by many factors like foods, medications, systemic disorders and disorders of the GI tract. Fifty to seventy percent of the patients with chronic dyspepsia do not have a focal or structural lesion identifiable at upper GI endoscopy. Dyspepsia requires detailed evaluation when there are alarm symptoms (Table 5.3).

Table 5.3: Alarm symptoms in dyspepsia

Weight loss	*Unexplained anemia*
Progressive dysphagia	Jaundice
Persistent vomiting	Lymphadenopathy
Gastrointestinal bleed	Palpable abdominal mass

NAUSEA AND VOMITING

Nausea is the subjective feeling of a need to vomit. *Vomiting* is the forceful expulsion of gastrointestinal contents orally resulting from the contractions of gut and thoracoabdominal wall musculature. It is a neurogenic response triggered by the chemoreceptors in the brainstem or reflexly through the irritation of stomach. Irritaton of the pharynx and upper esophagus by mechanical or chemical stimuli can evoke vomiting. Psychogenic factors lead to nausea and vomiting in many cases.

Regurgitation is effortless passage of gastric contents into the mouth.

Rumination is repeated regurgitation of stomach contents which may be rechewed and swallowed.

Vomiting consists of many phases such as nausea, hypersalivation, pallor, sweating and hyperventilation. Retching is an involuntary effort to vomit, which is followed by the expulsion of gastrointestinal contents through the mouth and sometimes through the nose. Vomiting unaccompanied by nausea is often called *projectile vomiting*. Vomiting is a common symptom in many gastrointestinal disorders and systemic illnesses. It is commonly seen in conditions associated with CNS diseases like increased intracranial tension (ICT), intracranial hemorrhage, brainstem lesions and others (Table 5.4).

Table 5.4: Important causes of vomiting

GI causes	*Non-GI causes*
Obstructive disorders	Cardiopulmonary
Pyloric stenosis	Cardiomyopathy, myocardial infarction
Intestinal obstruction	
Superior mesenteric artery syndrome	
GI infections	Labyrinthine diseases
Viral	Motion sickness
Bacterial	Labyrinthitis
Inflammatory diseases	Intracerbral disorders
Cholecystitis, pancreatitis	Abscess, hemorrhage, malignancy,
appendicitis, hepatitis	hydrocephalus, raised intracranial tension
Motility disorders	
Gastroparesis	Psychiatric illness
Intestinal	Depression, bulimia
pseudo obstruction	Postoperative
Functional vomiting	Drugs
Abdominal irradiation	Metabolic/endocrine ↑ toxins

Table 5.5: Drugs causing vomiting

Cancer chemotherapy	*Cardiovascular drugs*
Cisplatin	Digoxin
Dacarbazine	Antiarrhythmics
Nitrogen mustard	Antihypertensives
Etoposide	Beta blockers
Methotrexate	Calcium channel blockers
Cytarabine	Diuretics
5-Fluorouracil	
Tamoxifen	
Vinblastine	
Antimicrobials	Central nervous system drugs
Erythromycin	Antiparkinsonian drugs
Tetracycline	Anticonvulsants
Antituberculosis drugs	
Acyclovir	
Sulfonamides	
Gastrointestinal medications	Others
Sulfasalazine	Analgesics
Zathioprine	NSAIDs
	Antidiabetic drugs
	Oral contraceptives
	Antigout drugs
	Theophylline

Table 5.6: Metabolic and endocrine causes of vomiting

Pregnancy	Hypoparathyroidism
Diabetic ketoacidosis	Hyponatremia
Metabolic acidosis	Hyperthyroidism
Poisonings	Addison's disease
Hyperparathyroidism	Acute intermittent porphyria
Hypercalcemia of other causes	

Approach to vomiting: History helps to define the etiology of unexplained nausea and vomiting. Drugs (Table 5.5), toxins and GI infections commonly cause acute symptoms. Some established illnesses lead to chronic vomiting. Pyloric obstruction and gastroparesis produce late postprandial vomiting of undigested food. Emesis due to intestinal obstruction occurs later. In severe cases of gastroparesis, the vomitus may contain food residue ingested hours or even days previously. The following points should be taken into consideration about vomiting—onset, duration, relationship with food, nature of vomitus, evidence of systemic diseases and the emotional state (Table 5.6).

HEARTBURN (PYROSIS)

This is a sensation of warmth or burning pain felt retrosternally or substernally or in the epigastrium. This occurs particularly at night when the patient lies flat in the bed or on bending or stooping, during which the intra-abdominal pressure increases. Occasionally there is difficulty in distinguishing heartburn from angina pectoris.

A common cause of heartburn is reflux esophagitis, which is widely prevalent.

DIARRHEA

Passage of abnormally liquid and/or unformed stools at an increased frequency, relative to the patient's usual habits, constitutes diarrhea. Stool weight more than 200 g/day is considered as diarrhea as per Western standards. In Indian subjects, the quantity of stool is much more. Diarrhea can be classified according to the duration (Table 5.7).

Two common conditions that must be distinguished from diarrhea are:

1. Pseudodiarrhea which is the frequent passage of small volume of stool often associated with rectal urgency and generally seen irritable bowel syndrome (IBS) or proctitis.
2. Fecal incontinence is the involuntary discharge of rectal contents. This is most often caused by neuromuscular disorders or structural anorectal problems.

Tenesmus is the frequent attempts to defecate, often due to the feeling of loaded rectum or unpleasant anorectal sensation.

Diarrhea, though usually mild, can become acute and life threatening at times, e.g. cholera, inflammatory bowel disease (IBD), dysentery, food poisoning and others. In children, diarrhea is a common cause of death next only to respiratory infections, in developing countries (Table 5.8).

CONSTIPATION

Constipation refers to the persistent, difficult, infrequent or seemingly incomplete defecation.

Table 5.7: Classification of diarrhea

Acute	Acute in onset and lasting for less than 2 weeks
Persistent	Acute in onset and persisting for more than 2 weeks and less than 4 weeks
Chronic	Incidious in onset and persisting for more than 4 weeks

Table 5.8: Alarm features in diarrhea

Profuse diarrhea with dehydration
Grossly bloody stools
Fever >38.5ºC
Duration >48 hours without improvement
Recent antibiotic use
New community outbreaks
Associated severe abdominal pain in persons >50 years
Elderly patients >70 years
Immunocompromised patients

Table 5.9: Common causes of constipation

Colonic obstruction	Neoplasm, stricture, ischemia, diverticulae, inflammatory diseases
Anal sphincter spasm	Anal fissure, painful hemorrhoids
Irritable bowel syndrome	Constipation predominant, alternating type
Medications	Calcium channel blockers, antidepressants, anticholinergics, opioid agonists, iron supplements
Colonic pseudo obstruction	Slow transit constipation, megacolon
Disorders of rectal evacuation	Pelvic floor dysfunction, descending perineum syndrome, rectal mucosal prolapse
Endocrinopathies	Hypothyroidism, hypercalcemia, pregnancy
Psychiatric disorders	Depression
Neurological diseases	Parkinsonism, multiple sclerosis, spinal cord injury, raised intracranial tension in children Progressive systemic sclerosis Generalized muscle disease

Most persons have at least three bowel movements per week. In clinical practice, among caucasians passage of formed stools less often than three per week is taken as constipation. In Indian subjects, there is no hard and fast criteria since the dietary habits vary widely in different geographic regions. In general, failure to pass stool at least once in two days in persons who take normal food, can be considered as constipation, especially if associated with physical and psychological discomfort (Table 5.9).

Alteration of Bowel Habits

Alteration of bowel habits includes constipation and diarrhea. Constipation is more common in adults whereas in children it is diarrhea. It may be seen in irritable bowel syndrome and colonic malignancies.

Flatulence

This is the feeling of excessive wind, associated with belching, abdominal distension and passage of flatus per rectum. It is only infrequently associated with organic diseases. In normal persons 25 liters of air is passed involuntarily from the gastrointestinal tract through both ends without being noticed. Anxiety about the passage of wind makes the patient distressed and leads to aerophagy swallowing air and vague symptoms.

GASTROINTESTINAL BLEEDING

Bleeding from gastrointestinal (GI) tract may present in five ways (Table 5.10).

Table 5.10: Five ways of bleeding from GI tract

1. *Hematemesis:* Vomitus of fresh red blood or coffee ground material
2. *Melena:* Altered partly digested blood which makes the stool tarry and foul smelling
3. *Hematochezia:* Passage of bright red or maroon blood from rectum
4. *Occult GI bleed:* Not visible to the naked eye, but identified by testing for occult blood in faces or the presence of iron deficiency anemia
5. Symptoms of blood loss and anemia

Hematemesis indicates an upper GI site of bleeding. If the bleeding is slow and blood remain in contact with gastric acid for sometime the colour turns brownish black and is described as *coffee ground vomitus.*

The black tarry character of melena results from the partial digestion of blood to acid hematin or other hemochromes by bacteria. About 50 to 60 ml of blood is necessary to cause melena. Blood must remain in the intestinal lumen for about 6 to 8 hours to produce melena. Melena is usually the result of upper GI bleeding, but the source may be the distal part of the small intestine or even the ascending colon. Salts of bismuth and iron contained in medications may also give a blackish color to the stool, though not tarry. This has to be distinguished from melena (Table 5.11).

The risk stratification in patients with peptic ulcer bleeding is by using Rockall's scoring system. This consists of pre-and postendoscopic scores. Parameters include age, shock, comorbid conditions, diagnosis at the time of endoscopy and endoscopic stigmata of recent hemorrhage (Tables 5.12 and 5.13).

Score of 0 to 2 indicates excellent prognosis. Nine or more is associated with high risk of death.

Table 5.11: Important causes of upper GI bleeding

Ulcers of the stomach and duodenum
Varices in the esophagus and stomach
Mallory-Weiss tears
Gastroduodenal erosions
Erosive esophagitis
Neoplasms
Vascular lesions such as gastric antral vascular ectasia (GAVE)
Dieulafoy lesion*, portal hypertensive gastropathy (PHG), etc.
No source identified

* Dieulafoy lesion is the condition in which a dilated artery or arteriole surfaces into the mucosa and gives rise to bleeding. Common sites are the stomach, colon and small intestine

Table 5.12: Assessment of patients with upper GI bleed

Hemodynamic status	*Blood loss %*	*Severity of bleed*
Shock (resting hypotension)	20–25	Massive
Postural (orthostatic hypotension and tachycardia)	10–20	Moderate
Normal	<10	Mild

Table 5.13: Rockall's scoring system

Variable	*Score*			
	0	1	2	3
Age Shock	<60 SBP>100 PR<100	60–79 SBP>100 PR>100	80 and above SBP<100	- -
Comorbidity	No major comorbidity	No major comorbidity	Cardiac failure Ischemic heart disease or any major comorbidity	Renal failure Liver failure Disseminated malignancy
Diagnosis at time of endoscopy	Mallory-Weiss tear No lesion identified, No stigmata of recent hemorrhage (SRH)	All other diagnosis except malignancy	Malignancy of upper GI tract	-
Signs of recent hemorrhage (SRH)	None or dark spot only		Blood in upper GI tract Adherent clot Visible or spurting vessel	

Table 5.14: Forrest classification

Type I: Active bleeding	Ia: Spurting hemorrhage Ib: Oozing hemorrhage
Type II: Stigmata of recent hemorrhage	IIa: Non bleeding visible vessel IIb: Adherent clot IIc: Flat pigmentation
Type III: Clean based ulcer	

The Forrest classification of peptic ulcer bleed is used to classify the rate of rebleeding (Table 5.14).

HEMATOCHEZIA

If the blood is bright red and is separates from the stool, it usually indicates a source in the sigmoid colon, rectum or anal canal, hemorrhoids being the commonest cause. If the blood is dark red and mixed with the stools, this usually indicates a source above the rectum. Carcinoma is the most important cause. Approximately 10% of the patients with rapid bleeding from an upper GI source present with hematochezia (Table 5.15).

Table 5.15: Differentiation between upper and lower GI bleed

Features	*Upper GI bleed*	*Lower GI bleed*
Site	Above the ligament of Treitz	Below the ligament of Treitz
Presentation	Hematemesis /melena	Hematochezia
Nasogastric aspiration	Blood	Clear fluid
Blood urea nitrogen /Creatinine ratio	Increased (>25:1)	Normal (<25:1)
Bowel sounds	Hyperactive	Normal

ABDOMINAL PAIN

This is the most common and important symptom by which patient presents to a gastroenterology clinic (Tables 5.16 and 5.17).

Types of abdominal pain:

1. Parietal pain arises from the abdominal wall, peritoneum or surface of solid organs—steady and aching in character and is located over the inflamed area. The pain of peritoneal

Table 5.16: The following details about the pain must be asked for

1. Site	6. Duration
2. Mode of onset	7. Frequency
3. Intensity	8. Aggravating or relieving factors
4. Character and constancy	9. Associated features
5. Areas of radiation	

Table 5.17: Characteristics of pain arising from important intra-abdominal organs

Peptic ulcer	Epigastric, burning or gnawing, meal related, wakes the patient, relieved by antacids
Gastric cancer	Epigastric, severe, partly meal related, not relieved by antacids
Pancreatic	High epigastric, severe, felt front to back, immediately after eating, relieved by sitting forwards
Midgut	Periumbilical, colicky, some relation to meals
Lower gut	Periumbilical or suprapubic, colicky, some relief from bowel action
Biliary	Right upper quadrant, severecolicky (over long time period), radiates to right shoulder, accompanied by nausea
Renal colic	Loin to groin, colicky (shorter duration compared to biliary colic), very severe, accompanied by nausea
Functional	Anywhere in the abdomen, colicky, accompanied by bloating, relieved by bowel action

inflammation is aggravated by pressure or changes in tension of the peritoneum.
2. Visceral pain arises from lesions of solid organs—dull, poorly localized pain, as visceral nerve supply is multisegmental. This pain is due to stimulation of visceral nociceptors.
3. Colicky pain is intermittent pain due to obstruction of a hollow viscus.
4. Referred pain is the pain felt in areas remote from the diseased organs.

ACUTE ABDOMEN

This term is used generally to indicate severe acute painful lesions in the abdomen not responding to usual mild analgesics, often caused by surgical or less frequently medical conditions. Delay in diagnosis and management leads to rapid deterioration and severe morbidity or death. Such conditions have to be managed as emergencies (Table 5.18).

Abdominal Distension

This is the complaint given by the patients to denote either a feeling of fullness after ingestion of food without actual distension of abdomen or actual increase in girth. The former is often associated with diseases like gastritis, biliary or pancreatic diseases or malabsorption states. Actual distension of the abdomen is caused by the 5 Fs—fat, fluid, flatus, fetus and feces. Abdominal wall and cavity are common sites of deposition of fat. Prolonged constipation and accumulation of gas and feces in the intestine occur characteristically in intestinal obstruction. The distension will be obvious on inspection of the abdomen. Distension of the stomach hypochondrium. Collection of free fluid in the peritoneal cavity is called ascites. Fluid present within cysts such as ovarian cyst, fluid walled off by inflammatory adhesion in the peritoneal cavity, hydatid cysts and congenital cystic diseases of kidney and liver give rise to localized abdominal swelling. In women of child bearing age pregnancy is the commonest cause of abdominal distension. Enlargement of solid organs causes localized masses in their anatomic regions. But when the enlargement is gross, these masses may occupy almost the whole of the abdomen, e.g. hepatomegaly, splenomegaly.

Table 5.18: Causes of acute abdomen

Acute appendicitis	Acute mesenteric ischemia
Acute cholecystitis	Abdominal aortic dissection/rupture
Acute pancreatitis	Obstructed hernias
Acute diverticulitis	Gynecological
Perforated peptic ulcer	Ruptured ectopic pregnancy
Small bowel obstruction	Twisted ovarian cyst

Note: Medical conditions such as diabetic ketoacidosis, acute intermittent porphyria, poisonings and psychiatric conditions like Munchausen syndrome may masquerade as acute abdomen

JAUNDICE

Jaundice/icterus is the yellowish discoloration of tissue resulting from deposition of bilirubin. Tissue deposition of bilirubin occurs only in the presence of serum hyperbilirubinemia. It is a sign of liver disease or hemolytic disorder. Less commonly it may be a manifestation of obstruction to drainage of bile into the intestine as occurring in tumors of the pancreatic head or biliary stones.

Approach to Jaundice

A detailed history is the single most important part of the evaluation of a patient with jaundice. Important aspects include the presence of prodromal symptoms which favors infective etiology such as viral hepatitis. In endemic areas liver involvement due to infections such as Weil's disease and malaria should also be considered. History of intake of drugs including complimentary or alternate system medicines and parentral drug exposures including transfusions and tattoos should be asked for. Other important questions include travel history, exposure to people with jaundice, possibly contaminated foods, occupational exposure to hepatotoxins, sexual exposure and alcohol consumption. The duration of jaundice and any accompanying symptoms like arthralgia, myalgia, rash, anorexia, weight loss, abdominal pain, fever, pruritus and changes in the color of urine and stool should be enquired. Pruritus and clay colored stools are associated with cholestasis. Jaundice with GI bleed occurs in chronic liver disease with portal hypertension and hemobilia. Jaundice associated with severe right upper quadrant pain and shaking chills suggests choledocholithiasis and ascending cholangitis.

PRURITUS (ITCHING)

It is defined as a sensation that elicits the desire to scratch. Pruritus may be localized or generalized. Local causes usually include primary skin disorders. Generalized pruritus may accompany cholestatic jaundice (obstructive jaundice). Presence of excess

Table 5.19: Systemic conditions associated with pruritus

Cholestasis	Thyroid disease
Malignancy	Polycythemia vera
Chronic renal disease	Delusions of parasitosis
Pregnancy	Drug reactions

bile salts in blood may be the cause of this symptom. In many cases, the severity of jaundice and extent of pruritus do not directly correlate. Several other systemic diseases (lymphomas, chronic kidney disease, allergic conditions and others also lead to generalized pruritus) (Table 5.19).

STEATORRHEA

It is defined as the passage of pale, bulky stool containing excess of fat, that commonly floats in water and difficult to flush away from the toilet. Quantitatively steatorrhea is defined as stool fat exceeding 7 g per day. In the Indian context, stool tends to stick to the hand and have a greasy feel after normal washing (Table 5.20).

CONSTITUTIONAL SYMPTOMS IN GI DISEASES

Anorexia: This term refers to loss of appetite. It often indicates an important pathology, particularly in the upper GI tract. Appetite and metabolism are regulated by a delicate network of neural and hormonal factors. Hypothalamic feeding and satiety centers play a central role in these processes (Tables 5.21 to 5.23).

Table 5.20: Causes of steatorrhea

Intraluminal maldigestion
Chronic pancreatitis
Cystic fibrosis of the pancreas
Pancreatic duct obstruction
Somatostatinoma
Small intestinal bacterial overgrowth (SIBO)
Mucosal malabsorption
Celiac disease
Tropical sprue
Whipples's disease
Abetalipoproteinemia
Postmucosal lymphatic obstruction
Congenital intestinal lymphangiectasia
Acquired lymphatic obstruction

Table 5.21: Central controllers of appetite

Increases	*Decreases*
NPY (Neuropeptide Y)	MSH (Melanocyte stimulating hormone)
MCH (Melanin concentrating hormone)	CART (Cocaine and Amphetamine related transcript)
AgRP (Agouti related peptide)	GLP-1 (Glucagon-related peptide)
Orexin	Serotonin
Endocannabinoid	

Table 5.22: Causes of anorexia

Local causes	Gastritis Gastric lymphoma Gastric carcinoma and other upper GI malignancies Gastric ulcer Atrophic gastritis
Systemic illnesses	Infections like tuberculosis Cirrhosis, hepatic failure, renal failure Drugs like fenfluramine
Psychological factors	Anxiety Depression Anorexia nervosa

Table 5.23: Excessive appetite occurs in

Diabetes mellitus
Thyrotoxicosis
Hypothalamic disorders
Certain forms of depressive psychosis
Drugs like corticosteroids and antihistamines

Many gut peptides, hormones, metabolites, and cultural and psychosocial factors also influence the regulation of appetite.

Weight Loss

Unintentional loss of 10% of body weight over 6 to 12 months is significant. Mechanisms of weight loss include decreased food intake, malabsorption, loss of calories and increased energy requirement (Tables 5.24 and 5.25).

Fever

Fever may be associated with GI infections, hepatitis, cholangitis, lymphoma and others.

Table 5.24: Mechanisms of weight loss

Decreased caloric intake	*Caloric loss*	*Increased energy expenditure*
Socioeconomic factors (poverty) Anorexia Medications Difficulty in eating (surgical conditions) Cytokines Depression/dementia	Malabsorption	Hypermetabolic states Movement disorders Excessive exercise

Table 5.25: Causes of unexplained weight loss

Depression/anxiety
Chronic pain or sleep deprivation
Psychosocial deprivation/malnutrition in the elderly
Existing conditions like COPD/cardiac failure, diabetes mellitus hyperthyroidism
Occult malignancies in the proximal colon/renal/lymphoma
Anorexia nervosa in atypical group, e.g. young men
Endocrine diseases like Addison's disease, panhypopituitarism

CHAPTER

6 Physical Examination of the Alimentary System

KR Vinaya Kumar

General examination, Oral cavity, Physical examination of the abdomen, Surface marking of the abdominal organs, Palpitation, Percussion, Auscultation of the abdomen, Examination of the genitalia, Anus and rectum, Appendix-1: Clinical points to identify abdominal masses, Appendix-2: Common causes of enlargement of abdominal organs

GENERAL EXAMINATION

Nutritional Status (Tables 6.1 to 6.4)

Proper nutrition depends on normal function of the alimentary tract. Diseases which lead to vomiting, diarrhea or dysphagia lead to starvation and severe malnutrition. Bleeding from benign and malignant ulcers lead to iron deficiency anemia, e.g. carcinoma stomach, inflammatory bowel diseases, hemorrhoids and others. On the other hand, several nutritional disorders such as kwashiorkor and pellagra lead to diarrhea.

There is no single tool that is an accurate predictor of nutritional status. The subjective global assessment (SGA), a comprehensive nutritional

Table 6.1: Subjective global analysis (SGA)

History
Weight change
Dietary change
Gastrointestinal symptoms
Functional capacity
Disease and relation to nutritional requirements
Physical examination
Subcutaneous fat
Muscle wasting
Ankle edema
Sacral edema
Ascites
SGA rating
A—Well nourished
B—Moderately malnourished
C—Severely malnourished

Table 6.2: Body mass index and body habitus

<18	Underweight
18-25	Ideal weight
>25-30	Overweight
>30-40	Obese
>40	Super obese

Table 6.3: GI causes of clubbing

Cirrhosis of liver, amebic abscess liver
Inflammatory bowel diseases
GI malignancy

Table 6.4: Peripheral stigmata of chronic liver disease (CLD)

• Alopecia
• Parotid enlargement
• Fetor hepaticus—characteristic sweet smelling breath
• Palmar erythema seen on thenar and hypothenar eminence often with blotchy appearance
• Leukonychia—nail appears pale and opaque
• Dupuytren's contracture—usually affects palm and rarely plantar fascia. There is localized thickening of palmar fascia mainly on the medial part, which leads to flexion of ring finger and to some extent the little finger. Exact cause is not known.
• Bruising, gynecomastia, paucity of axillary and pubic hair
• Spider naevi—small telangiectatic superficial blood vessels with central feeding vessel—an arteriole
• Asterixis (flapping tremor)—failure to actively maintain posture or position
• Eye signs mimicking hyperthyroidism
• Signs of chronic cholestasis
• Pruritus
• Scratch marks
• Xanthelasma
• Clubbing
• Shiny nails

assessment can be used to categorize the patients as well as nourished and malnourished individuals.

Body mass index (BMI) also be used to categorize patients according to their nutritional status (Refer Chapter 2)

PALLOR

Anemias resulting either from chronic blood loss or malabsorption of hematinic factors are frequent accompaniments of chronic gastrointestinal disorders.

Jaundice/Icterus

Jaundice can be detected by examining the sclera which has a particular affinity for bilirubin, due to its high elastin content. Scleral icterus indicates serum bilirubin of at least 3 mg/dL (Fig. 6.1). Other sites such as under aspect of the tongue, skin over the palms and other tissues should be examined preferably in direct or artificial sunlight.

Differential diagnosis is yellowish staining of the skin seen in carotinoderma which (spares sclera) and exposure to quinacrine or phenol.

Hemolytic jaundice leads to a lemon yellow tinge. In obstructive jaundice, the color is dark yellow or with an orange tinge. There may be scratch marks due to itching evoked by bile salts.

Cyanosis

Hepatopulmonary syndrome can lead to central cyanosis less commonly. Vast majority of cyanosis are caused by cardiac, respiratory and other diseases.



Fig. 6.1: Jaundiced sclera in moderately severe jaundice. *Note:* The level of serum bilirubin and depth of icterus do not directly correlate

Clubbing

Gastrointestinal and hepatic disorders may lead to digital clubbing at times.

Lymphadenopathy

Generalized lymphadenopathy is seen in lymphoma, metastatic GI malignancies and primary biliary cirrhosis. Enlarged left supraclavicular lymph node in GI malignancies such as carcinoma of stomach is known as Troisier sign (Virchow's glands).

Pedal Edema

Pedal edema caused by hypoalbuminemia is seen decompensated hepatic liver cirrhosis and malabsorption states. Inferior vena caval (IVC) obstruction may develop in hepatic tumors and less commonly in thrombophilic states.

Prominence of Jugular Veins due to Raise in Jugular Venous Pressure (JVP)

If the cause of ascites is right-sided heart failure, the JVP will be raised and hepato jugular reflux can be elicited. In Budd-Chiari syndrome, hepato jugular reflux will be absent due to obstruction to the hepatic veins.

Asterixis is caused by the abnormal function of motor centers that regulate the tone of the agonist and antagonist muscles normally involved in maintaining posture. This can be elicited by two methods:

1. *Classic method:* Elicited by dorsiflexion of the patient's hand, with arms outstretched and fingers separated. The postural lapse that occurs consists of a series of rapid, involuntary, flexion-extension movements of the wrist.
2. *Alternative method:* Ask the patient to clench his fingers around the examiner's fingers. Asterixis can be appreciated by the subtle movements of the patient's wrist.

Constructional apraxia is the phenomenon in which the patient is not able to perform complex acts requiring sequential regulated action, in the absence of any demonstrable motor paralysis. This can be seen in minimal hepatic encephalopathy. Constructional apraxia can be elicited with Reitan number connection test (Refer Neurology).

Other Clinical Signs that may be Seen in GI Disorders

Signs of Malabsorption

Malabsorption has to be suspected in a person who loses weight despite taking adequate amounts of

food and in the vast majority of cases associated with large bulky greasy stools with or without diarrhea. Malabsorption leads to nutritional deficiencies characterized by Bitot's spots, stomatitis, angular cheilitis, aphthous ulcers, acrodermatitis, hyperkeratosis, muscle wasting, koilonychia and others.

Other findings picked on general examination which point to gastrointestinal disease include pigmentation of the lips in Peutz-Jeghers syndrome, Kayser-Fleischer ring in Wilson's disease, leg ulcers in inflammatory bowel disease, lipemia retinalis in diabetic ketoacidosis, Purtschers retinopathy (discrete flame-shaped hemorrhages with cotton wool spots) seen in acute pancreatitis and others.

Malignancy of internal organs may give rise to superficial markers. This include:

Acanthosis nigricans: It is the velvety hyper-plasia and hyperpigmentation of the skin of the neck, axillae, hands, genitalia and oral mucosa, associated with intra-abdominal adenocarcinomas, commonly carcinoma of stomach.

Sweet's syndrome (acute febrile neutrophilic dermatoses): It is associated with lymphoproliferative neoplasms.

Tylosis is the diffuse hyperkeratosis of the palms and soles which is associated with esophageal carcinoma.

EXAMINATION OF GASTROINTESTINAL ORGANS

Oral Cavity

Mouth and throat should be examined using a pen torch and tongue depressor. Examine systematically the inner and outer surfaces of the lips, angles of the mouth, gingiva, teeth, floor of the mouth, upper and lower surface of the tongue, tonsils, palate and pharynx. The tongue should be protruded to bring its posterior third into view. Gentle pressure on the anterior aspect of the relaxed tongue held in mouth will enable the inspection of the oropharynx, part of the nasopharynx and down to the epiglottis.

Swallowing has to be enquired into and any symptom of dysphagia and odynophagia has to be checked by making the patient swallow liquids and solids respectively. Since the esophagus is a deeply-placed structure, further investigation of esophageal diseases has to depend on contrast imaging (barium swallow) and endoscopy.

PHYSICAL EXAMINATION OF THE ABDOMEN REGIONS (FIG. 6.2)

Abdomen can be arbitrarily divided into 9 regions by two lateral vertical planes passing from femoral artery below to cross the costal margin close to the tip of ninth costal margins. Two horizontal planes the subcostal and inter-iliac, pass across the abdomen to connect the lowest points on the costal margin and tubercles of iliac crests respectively. Figure 6.2 gives the regions of the abdomen.

Inspection

Patient should be lying supine with the arms on the sides, on a couch or mattress, the head and neck supported by pillows comfortably. The examiner should stand or sit on the right side of the patient for further examination. The abdomen is exposed from just above the xiphisternum down to the level of symphysis pubis. Inspection of groins and genitalia should not be missed. While examining genitilia and anal region the patient should be informed of the procedure. Exposure of the genitilia and anal regions should be only for the minimum period and that too in privacy. It is well worth spending at least 30 seconds observing the abdomen from different positions to note the following features:

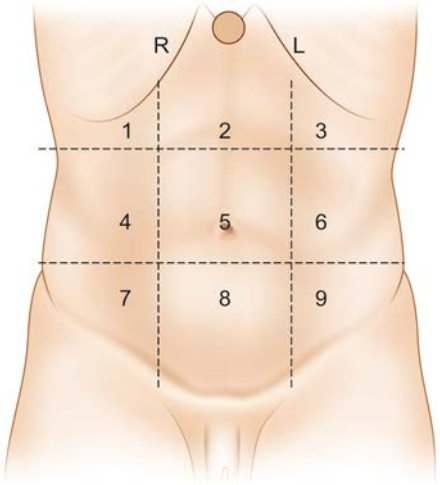


Fig. 6.2: Regions over the abdomen. (1) right hypochondrium, (2) epigastrium, (3) left hypochondrium, (4) right lumbar region, (5) umbilical region, (6) left lumbar region, (7) right iliac fossa, (8) hypogastrium, and (9) left iliac fossa

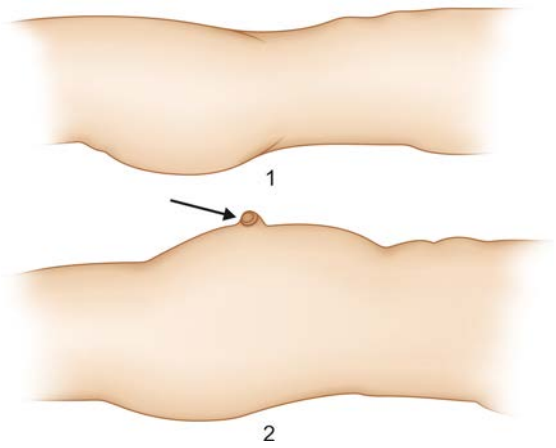


Fig. 6.3: Contour of abdomen. (1) Normal scaphoid (2) Distended with fluid—arrow shows everted umbilicus

Shape (Fig. 6.3)

Normal contour of the abdomen is scaphoid. Generalized fullness or distension is seen in obesity and ascites. Localized fullness which is symmetrical and centered around umbilicus is seen in small bowel obstruction. Asymmetrical fullness may be caused by organomegaly such as liver, ovary or other masses. Extremely sunken abdomen is seen in advanced starvation, malignancy and cachexia.

Umbilicus

Normal umbilicus is inverted and retracted. It is everted in umbilical hernia, vertical in pelvic or ovarian tumours and horizontal in ascites.

Movements of Abdominal Wall

Normally there is a gentle rise in inspiration and fall during expiration. Movements should be free and equal on both sides. In peritonitis the abdomen is still or silent.

Visible Pulsations

In normally nourished individuals pulsations other than the aortic pulsations are not visible. Abdominal aortic pulsations may be visible in the epigastrium. This may be felt as arterial pulse and is not expansile. It must be differentiated from aneurysm of abdominal aorta where the pulsations are more obvious, extensive and is felt on palpation (expansile pulsation).

Visible Peristalsis

Visible gastric peristalsis: Occurs when there is obstruction at the pylorus caused by stricture following duodenal ulceration or by carcinoma stomach. It is a wave of gastric peristalsis seen progressing from left hypochondrium and epigastric region towards the right lumbar region.

Visible intestinal peristalsis: Seen in distal small bowel obstruction. It is seen as a step ladder form of peristaltic waves, in the umbilical region.

In very thin, elderly persons with lax abdominal wall, visible gastric and intestinal peristalsis may be seen even without organic obstruction.

Skin and Surface of Abdomen

Striae gravidarum: These are white or pink wringled linear marks over the skin of the abdomen produced by gross stretching of skin and rupture of elastic fibers. It indicates recent change in size of abdomen like pregnancy, ascites and wasting diseases.

Purple striae are seen in Cushing syndrome or as a complication of prolonged corticosteroid therapy.

Scars: Their site and whether they are old (white) or recent (red or pink) should be noted. Thinned out scars are likely to be weak and they may be the sites for development of incisional hernias.

Pigmentation

Erythema ab igne is brown mottled pigmentation produced by constant application of heat usually by hot water bottle or heat pad. It may be a sign that the patient is experiencing severe ongoing pain such as trophic ulcers, chronic pancreatitis and other lesions.

Linea nigra is pigmentation in the midline below umbilicus, seen in pregnancy.

Grey Turner's sign is bluish discoloration of loins or flanks, seen in acute hemorrhagic pancreatitis.

Cullen's sign is bluish discoloration of periumbilical region seen in acute hemorrhagic pancreatitis.

Prominent Superficial Veins

In normal individuals, veins are not seen prominently over the abdominal wall. Their presence underlies abnormalities in drainage or underlying disease process. Thin veins over the costal margins are of no significance.

Classically distended veins over the abdominal wall occurs in portal hypertension (PHT) and

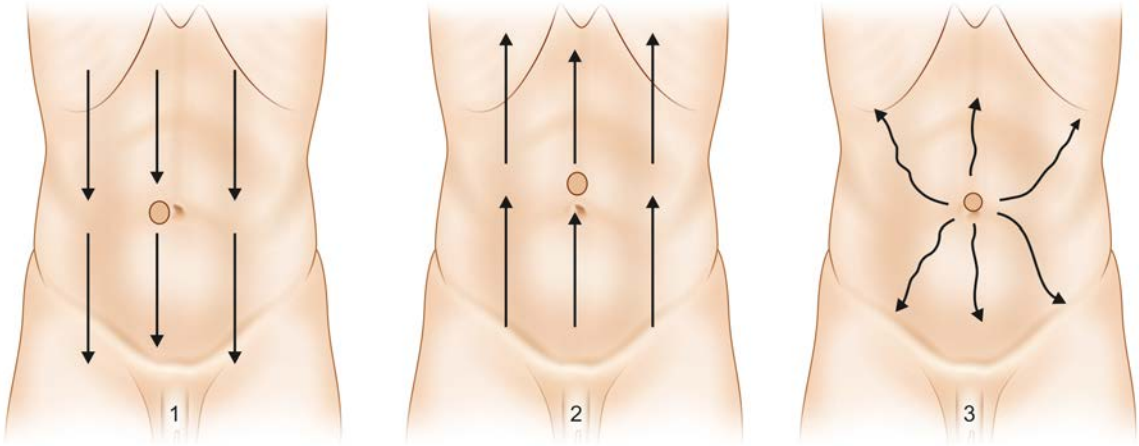


Fig. 6.4: Direction of blood flow in veins on the abdominal wall. (1) Obstruction to superior vena cava, (2) Obstruction to inferior vena cava, and (3) Obstruction to portal vein-caput medusae

obstruction to the inferior vena cava (IVC). The direction of blood flow in the veins should be noted. Distended veins radiating from the umbilicus indicates portal hypertension (the flow is away from the umbilicus). This is compared to the locks of hair of mythological dragon Medusa (Caput Medusae).

In inferior vena caval obstruction, distended veins develop over the abdomen and chest wall. These represent dilated anastomotic channels between superficial epigastric and circumflex iliac veins below, and lateral thoracic veins above, conveying the diverted blood from long saphenous vein to the axillary vein. The direction of flow is therefore upwards. If they are prominent, try to detect the direction of flow by occluding a vein, emptying it by massage and looking for the direction of refill (Fig. 6.4).

Uncover and Inspect both Loins and Genitalia

Abdominal Measurements

Abdominal girth should be measured at the level of waist. This is important in the diagnosis of obesity and metabolic syndrome.

Measure the distance between lower end of xiphisternum to the umbilicus and from umbilicus to the symphysis pubis. Normally umbilicus is at the center. Presence of mass in the upper abdomen stretches the upper half and vice versa.

Spinoumbilical measurement: It is the distance between umbilicus and anterior superior iliac spines on either side. Normally they are equal. It should be measured on both sides to find out the shift of umbilicus to one side, as in the case of tumors arising from the iliac fossae.

SURFACE MARKINGS OF ABDOMINAL ORGANS

Liver

Upper border of right lobe corresponds to the level of 5th rib, 2.5 cm medial to the right midclavicular line. Upper border of left lobe is at the level of 6th rib in the left midclavicular line. In males it corresponds to the line joining a point 1cm below the right nipple to a point 2 cm below the left nipple. Lower border runs obliquely from 9th right to 8th left costal cartilage crossing the midline halfway between the base of xiphoid process and umbilicus. The left lobe extends to the left of the sternum for about 5 cm.

Spleen

Situated behind 9th, 10th and 11th ribs with long axis along the line of 10th rib. Anteriorly it extends to midaxillary line, posteriorly its superior angle is 4 cm lateral to the 10th thoracic spine. It is separated from 9-11th ribs by the diaphragm.

Kidneys

Surface markings of kidney are indicated by Morris quadrilateral space on either side. Two parallel horizontal lines are drawn on the back at the levels of 11th dorsal and 3rd lumbar spines. They are intercepted by 2 vertical lines drawn 3.75 cm and 8.75 cm respectively from the midline. See Figure 28.1 in Section 10.

Gallbladder

Situated at the junction of 9th costal-cartilage and outer border of right rectus abdominis. Draw a line from left anterior superior iliac spine through the umbilicus. At the junction of this line and costal margin, is the gallbladder, provided the shape of abdomen is normal. This is called Grey Turner's method. Gallbladder is better seen than felt when enlarged.

PALPATION OF THE ABDOMEN

Successful palpation to get clinical evidence is an art combining deliberate effort, gentleness and proper method. To the patient, it often renders a healing touch' if done properly, if done otherwise it can be disturbing the patient and not fully effective in collecting information. The student should practice this art by constant effort.

Before starting palpation ask the patient to relax as best as he can and to breathe normally. Enquire about the site of pain. Palpation over this region can be reserved for the last so that pain caused by palpation does not vitiate further physical examination. While palpating, the wrist and forearm should be in same horizontal plane. Palpate gently with firm pressure exerted from the wrist, with the fingers held almost straight but with slight flexion at the metacarpophalangeal joints. Avoid sudden poking movements with fingertips. It is necessary to palpate in relation to the breathing movements of the abdomen, so that during inspiration the hand is relaxed in order to allow mobile organs to come down and touch the palpating hand. During expiration, the hand is gently pressed so as to reach deeper and known mobile organs. At times, if the patient is not fully cooperative palpation may have to be deferred. At times both the hands may be used one over the other to exert gentle but firm pressure, especially in obese subjects (Fig. 6.5).



Fig. 6.5: Palpation of the right hypochondrium for the lower border of the liver, and gallbladder

Start palpation from left iliac fossa. Palpate lightly and work anticlockwise to end in suprapubic region. The order of palpation of organs is listed in Table 6.5.

Alternatively palpation can be started from the right iliac fossa and continued in clockwise direction. All the organs in the upper abdomen except the pancreas move downward with inspiration and go up during expiration. Structures normally palpable are given in Table 6.6 and Figure 6.5.

All the organs in the upper abdomen move downward with respiration. Structures normally palpable are given in Table 6.6.

When a mass is palpable, assess the features listed in Table 6.7.

Table 6.5: Order of palpation

1. Left kidney
2. Spleen
3. Right kidney
4. Liver
5. Urinary bladder
6. Aorta, para-aortic glands and common femoral vessels
7. Palpate both groins
8. Examine the external genitalia

Table 6.6: Normally palpable structures in the abdomen

1. Aorta
2. Edge of the liver
3. Lower pole of right kidney
4. Hard feces
5. Normal colon
6. Small inguinal lymph nodes
7. Distended urinary bladder

Table 6.7: Characteristics of palpable masses

Site Size and shape	Mobility (capable of being moved by palpation)
Surface (smooth or otherwise)	Presence of tenderness (if so, severity)
Edge (sharp or rounded) Consistency	Movement with respiration (free or restricted)
(Soft, firm or hard)	Bimanually palpable/ ballotable/pulsations (if present, expansile or transmitted)

Palpatory Findings of Different Organs (Fig. 6.6)

Liver

Place the flat of the hand parallel to the right subcostal margin lateral to the rectus abdominis with fingers pointing upwards towards the ribs. Exert gentle pressure and ask the patient to breathe in deeply. Palpate for the edge of the liver which can be felt moving downwards and under the examining hand. Repeat this from lateral to medial regions to trace the liver edge as it passes upwards to cross from right hypochondrium to epigastrium.

Alternatively, place the right hand below and parallel to the right subcostal margin. The liver edge will then be felt against radial border of the index finger. Avoid placing hand over rectus abdominis. Do not begin palpation too close to costal margin.

The normal liver is often palpable even without enlargement. Hepatomegaly measured in centimeters below the right costal margin, which should be measured with a tape for documentation (Fig. 6.6). Assess the character of liver surface, whether smooth, irregular or nodular. Comment on the consistency, whether it is soft, firm or hard. Look for any tenderness (Table 6.8) or pulsations (Fig. 6.7).

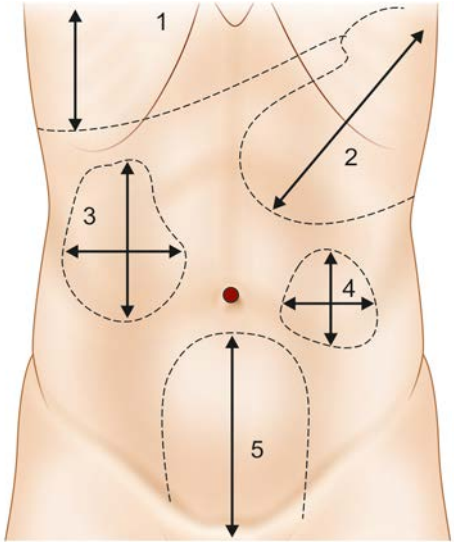


Fig. 6.6: Position of abdominal organs, the arrows indicate their direction of enlargement and lines for measurement. (1) liver (2) spleen (3) kidney (4) colonic mass (5) uterus



Fig. 6.7: Palpation of the liver for expansile pulsation

Table 6.8: Causes of hepatomegaly

Soft, smooth, tender liver	Congestive cardiac failure, acute viral hepatitis, amebic hepatitis, cholangitis, septic conditions
Firm and regular	Fatty liver/chronic obstructive jaundice Early stages of cirrhosis
Firm and irregular	Cirrhosis
Nodular	Hepatoma-advanced secondary carcinoma, some types of cirrhosis
Pulsatile expansile	Systolic-tricuspid regurgitation, diastolic-tricuspid stenosis
Pulsatile transmitted	From aorta and other major vessels

A congenital variant of the right lobe projecting down lateral to the gallbladder called Reidel's lobe, may be mistaken for gallbladder itself or right kidney.

Gallbladder

Normal gallbladder cannot be felt by the palpating hand. Enlarged gallbladder is felt as a firm, smooth, or globular swelling with rounded borders, just lateral to the edge of the rectus abdominis near the tip of the ninth costal cartilage. It moves with respiration.

Its upper border merges with the lower border of the right lobe of the liver. It is not bimanually palpable. At times, the gallbladder may occupy different locations such as right lumbar region or even right iliac fossa, when grossly enlarged. It may also become mobile (Table 6.9).

Table 6.9: Painless enlargement of the gallbladder occurs in

1. Carcinoma head of pancreas or other malignant causes of obstruction to common bile duct (CBD) below the entry of cystic duct
2. Mucocele of gallbladder
3. Carcinoma of gallbladder

Courvoisier's Law

In a patient with jaundice, a palpable gallbladder makes gallstone obstruction of CBD an unlikely cause. In cholelithiasis, the gallbladder wall is diseased, thickened, contracted, therefore it is non-distensible.

Murphy's Sign

Ask the patient to breathe deeply and palpate for gallbladder as usual. At the height of inspiration the breathing stops with a gasp in patients with cholecystitis. This represents the underlying acutely inflamed gallbladder walled off by greater omentum.

Spleen

The spleen is not normally palpable. To become palpable, spleen should have enlarged 2-3 times the normal size. It is felt beneath the left subcostal margin. Enlargement takes place in a superior and posterior direction before it becomes palpable subcostally. Direction of enlargement is towards right iliac fossa. Place the flat of the left hand over the lowermost part of the rib cage posterolaterally, thereby restricting the expansion of lower ribs on inspiration. The right hand is placed beneath the costal margin well out to the left. Ask the patient to breathe deeply, and exert gentle pressure with the fingers of the right hand beneath the costal margin, at the same time applying pressure medially and downwards with the left hand. Repeat this, with the right hand moving more medially beneath costal margin on each occasion. If the spleen is still not palpable, put the patient on right lateral position with the left hip and knee flexed, support the lower ribs and the repeat the examination as above. Since the spleen falls forward as the abdominal muscles are more relaxed in this position, even mild enlargement can be detected (Fig. 6.8).



Fig. 6.8: Palpation of spleen with the patient lying in the right lateral position with thigh flexed

Middleton's Maneuver

This is an alternate method to palpate the spleen. The examiner stands on the left side of the patient, facing the foot of the bed. The hooked fingers of the left hand are placed under the costal margin and with the right hand, pressure is exerted over the posterolateral aspect of the lower thorax. Patient is made to take deep breath. Spleen is felt at the end of deep inspiration. Splenomegaly may be mild (1–2 cm), moderate (3–7 cm), or large (> 7cm).

In mild splenomegaly, the spleen will be present as a soft or firm swelling with smooth, rounded borders. When moderately or grossly enlarged it can be felt as a firm swelling in the left upper quadrant of abdomen. It moves with respiration. The direction of movement is towards the right iliac fossa (Fig. 6.6). It is dull on percussion. The upper border is not palpable. Splenic notch or (notches) can be palpated in the lower medial border if splenomegaly is moderate or large.

Moderate to large splenomegaly occurs more commonly. This occurs in portal hypertension, chronic leukemia, acute leukemia's, lymphomas, subacute or relapsing infections (typhoid fever, infective endocarditis, malaria, brucellosis, relapsing fevers and others) (Table 6.10).

Mild splenomegaly occurs in acute infective fevers, macrocytic anemia, hemolytic states and less commonly in iron deficiency anemia as well.

Table 6.10: Diseases associated with massive splenomegaly

Chronic myelogenous leukemia	Gaucher's disease
Lymphomas	Chronic lymphatic
Hairy cell leukemia	Leukemia
Myelofibrosis with myeloid	Sarcoidosis
Metaplasia	Autoimmune
Polycythemia vera	Hemolytic anemia
Hemoglobinopathies	Diffuse splenic
Thalassemia	Hemangiomatosis Chronic malaria, leishmaniasis



Fig. 6.9: Bimanual palpation of right kidney
See text for details

Kidneys

Bimanual technique is used for palpating kidneys.

Left kidney

Place the left hand posteriorly in the left loin and the other in the left lumbar region. Ask the patient to take deep breath, push the two hands firmly. The left kidney is usually palpable. Lower pole, when palpable, is felt as a rounded firm swelling between both right and left hands (bimanually palpable), and it can be pushed from one hand to other (ballotable).

For the right kidney, the same technique is used on the right lumbar region (Fig. 6.9 and Table 6.11).

Table 6.11: Clinical differentiation between spleen and left kidney

	Spleen	*Left kidney*
Location	Anterior, 9-11th ribs	Posterior
Notch	Present	Absent
Edge	Sharp	Rounded
Enlargement	Towards right iliac fossa	Towards lumbar region
Insinuation of fingers between the costal margin and the organ	Not possible	Possible
Movements with respiration	Moves freely	Restricted
Band of colonic resonance	Absent	Present
Mass characteristics	Not ballotable or bimanually palpable	Ballotable and bimanually palpable
Upper border	Cannot be felt	Can be felt
Fullness of loin	Absent	Present

Note: All these characteristics change if the splenomegaly is massive, i.e. more than 15 cm palpable

Urinary Bladder

Normally urinary bladder is not palpable when empty. In thin individuals, even a normally distended bladder is visible and palpable. It is palpable as a smooth, firm, regular, oval-shaped swelling in the suprapubic region and its dome may reach even as far as the umbilicus (Table 6.6). The borders are rounded. The lateral and upper border can be readily made out, lower border cannot be felt. In normal persons, the mass disappears on micturition. It should be differentiated from:

1. *Gravid uterus:* It is firmer, mobile side-to-side and is felt as a solid persistent mass.
2. *Fibroid uterus:* When the size is moderate or large the uterus may be palpable to varying heights above the symphysis pubis. The uterus is firm, nontender and irregular in contour.
3. *Ovarian cysts:* These presents as a mass (at times bilateral) in the iliac region lateral to the midline. They are rounded or irregular, firm or cystic and mobile in most cases. They may reach large sizes almost filling the abdomen at times.

Examination of Groins, Para-aortic Nodes and Vessels

Examine the Groins for Hernia

Palpate aorta and common femoral vessels with the finger tips. Aorta is detected by deep palpation a little above and left of the umbilicus. Palpate with the extended fingers of both hands, held side-by-side deeply into the abdominal wall. Remove both hands and repeat a few centimeters to the right. In this way the pulsation and width of the aorta can be estimated.

The common femoral vessels are palpable just below the inguinal ligament, at the midpoint between anterior superior iliac spine and symphysis pubis.

Lymph nodes lying along the aorta are palpable only when they are considerably enlarged and in thin subjects. They are felt as rounded, firm, often confluent, fixed or mobile masses in the umbilical region and epigastrium along the left border of the aorta.

PERCUSSION OF THE ABDOMEN

Percussion over solid organs gives dull note, whereas percussion over gas filled organs (hollow

viscera) give hyper resonant (tympanic) note. Most part of the abdomen is resonant, except over the liver, where the note is dull. Resonant percussion note over suspected enlargement of liver or spleen weighs against this possibility. In obese patients tympanic areas of abdomen may not give a truly resonant percussion note and palpation of organs is more difficult.

Defining Boundaries of Abdominal Organs

Liver (Table 6.12)

Upper and lower border of right lobe of liver can be mapped out by percussion. Start anteriorly at the 4th right intercostal space where the note will be resonant due to air in the lungs. Proceed vertically downwards. In normal liver, the upper border is at 5th right intercostal space where the note is dull. This extends down to the lower border at or just below the right subcostal margin. The normal span is 12 cm, extending from fifth right intercostal space to the palpable lower border or right costal margin (Fig. 6.10). In the normal subjects the upper border of the liver which can be made out by percussion moves down and upwards with inspiration and expiration (tidal percussion).

Serial examination can demonstrate changes in liver size. The enlargement of the liver is expressed in centimeters below the right costal margin or as enlargement of its span.

Spleen

Normal spleen is not palpable per abdomen except in very thin individuals, the patient lying in the left lateral position. But the splenic dullness can be percussed out in normal individuals. Enlarged spleen can be made out by palpation and percussion. Percussion of splenic dullness is accomplished with any of these three techniques:

1. *Nixon's method:* The patient lies on the right side so that the spleen lies above the colon and stomach. Percussion begins at the lower level of pulmonary resonance in the posterior axillary line and proceeds diagonally along a perpendicular line toward the lower mid-anterior costal margin. Dullness >8cm in an adult indicates splenic enlargement.
2. *Castell's method:* With the patient lying supine, percussion in the lower intercostal space in the anterior axillary line (8th or 9th) produces a resonant note if the spleen is normal in size. This is true during expiration or full inspiration. A dull percussion note on full inspiration suggests splenomegaly.

 The sensitivity of palpation and percussion for spleen is about 56 to 71% and 58 to 82% respectively.
3. *Percussion of Traube's semilunar space:* The Traube's space is an area of hyper-resonance on percussion in the left lower hemithorax caused by air in the stomach. The borders of space are 6th rib superiorly, the left mid axillary line laterally, and the left costal margin inferiorly.

Method: The patient is made to lie supine with left arm slightly abducted and breathe normally. Traube's space is percussed from medial to lateral margins, yielding a normal resonant sound. Dullness on percussion or reduction in the area of resonance suggest splenomegaly. This finding is not fully reliable, since several other organs may encroach on the Traube's space.



Fig. 6.10: Percussion of the lower border of the liver from above downwards. See text for details

Urinary Bladder

The distended bladder is dull on percussion and can be outlined as an oval mass above the symphysis pubis.

Table 6.12: The upper border of the liver may be obliterated in

- Emphysema
- Right sided pneumothorax
- Pneumoperitoneum (free air in the peritoneal cavity)

Detection of Ascites

Ascites is defined as the presence of excess free fluid in the peritoneal cavity. Normal peritoneal cavity contains a small amount (up to 100–200 mL) of serous fluid. In several pathological states, free fluid (transudate or exudate) accumulates and becomes clinically detectable when the quantity exceeds 1 liter or more.

Ascites can be detected by eliciting *shifting dullness* (Figs 6.11A to E).











Figs 6.11 A to E: Eliciting shifting dullness by percussion

A. Percussion note in the midline is resonant.
B. Dullness due to fluid in the right flank is percussed out in the supine position.
C. Dull area becomes resonant when the fluid moves down when the patient turns to the left.
D. The dullness due to fluid when the patient turns to the left is defined.
E. On turning to the right the area of dullness becomes resonant.

Shifting Dullness

The cardinal sign created by large quantities of free fluid (>1.5 L) is shifting dullness. With the patient lying supine, place the pleximeter finger along the longitudinal axis on the midline near the umbilicus and begin percussion moving the fingers laterally towards the right flank. When the dullness is first detected, keep the fingers in that position and ask the patient to roll on his left side. Wait for a few seconds for any peritoneal fluid to redistribute and the intestine to float up. If ascites is present, the percussion note becomes resonant. The shift in the area of dullness can be confirmed by finding the lower border of dullness with the patient still on his left side and seeing whether it shifts when the patient returns to the supine position, or turns to the right (Figs 6.11A to E).

Fluid Thrill

Vibrations caused by tapping the abdomen in tense ascites will be transmitted across the fluid to the opposite side. These vibrations (called fluid thrill) can be appreciated by palpation. At least 2000 mL of free fluid should be present to elicit this thrill.

Method: Sharply tap the abdomen at the flank by the fingers of the right hand while palpating the opposite flank with the left palm. Thrill can be appreciated At times when the abdomen is fatty the adipose layer may transmit the thrill. This is avoided by placing the patient's hand on the abdomen to interrupt the vibrations. An alternate method is to elicit the thrill diagonally in which direction the adipose layer does not transmit the thrill. This sign may not always be reliable.

Puddle Sign

This sign is elicited to detect the presence of mild ascites around 250 mL. It can be elicited by percussion or ausculto-percussion in the knee elbow position in which the anterior abdominal wall becomes most dependent and even small quantities of fluid collect around the umbilicus and produce dullness.

Method

1. *Percussion:* The patient is made to lie in the prone position for five minutes and then assume the knee elbow position. Dullness to percussion around the umbilicus is evidence of fluid collection. Previously resonant area becomes dull even if only a small amount of fluid is present.
2. *Auscultation:* Place the stethoscope over the umbilical region and scratch the abdominal wall from periphery towards umbilicus. A change in the quality of sound is noted while crossing the fluid margins. This sign is false positive in massive splenomegaly and distended urinary bladder. With the easy availability of ultrasound scan, this cumbersome manouver has lost its importance.

Hydatid Thrill

This technique is used for the percussion of cysts. Keep three fingers firmly over the cysts and percuss over the middle finger which is held firmly in position. A characteristic thrill is felt in hydatid cyst. Percussion displaces daughter cysts, which sink and when they come back to the cyst wall, a characteristic sensation is felt. This is hydatid thrill.

AUSCULTATION OF THE ABDOMEN

The following findings are looked for by auscultation:

1. Bowel sounds
2. Succussion splash
3. Arterial bruit
4. Venous hum
5. Friction rubs.

Bowel Sounds

The stethoscope should be placed on one site on the abdominal wall (just to the right of the umbilicus is the best) and kept until the sounds are heard. Normal bowel sounds are heard as intermittent low or medium pitched gurgles interspersed with an occasional high pitched noise or tinkle. Bowel sounds heard with unaided ear are called borborygmi. Increased bowel sounds with colicky pain is pathognomonic of small bowel obstruction. In between bouts of colicky pain, the bowel is quiet and no sounds are audible (Table 6.13).

Table 6.13: Abnormalities of bowel sounds on auscultation

Increased bowel sounds	*Absent bowel sounds*
Small bowel obstruction	Paralytic ileus
Malabsorption	Peritonitis
Severe GI bleeding	
Carcinoid syndrome	

Table 6.14: Causes of succussion splash

Succussion splash seen in
Pyloric stenosis
Advanced intestinal obstruction
Paralytic ileus
Normal stomach within two hours after the meal

Succussion Splash

This is the splashing sound heard over moderate or large quantity of fluid collected in a distended viscus such as stomach. While auscultating over the epigastrium with the patient lying supine, roll the patent briskly from side-to-side. In the presence of free fluid in stomach or other hollow viscera a splashing sound will be heard (Table 6.14).

Bruit

Bruit is an arterial turbulence produced when the blood flow is excessive or when the artery is narrowed and the flow is irregular. Listen for bruit by applying the stethoscope lightly over the abdomen. If an arterial bruit is heard, it indicates increased flow in the underlying vessel or stenosis or aneurysm. An epigastric bruit can be appreciated in 20% of healthy thin young adults especially if the auscultation is performed after a meal. Other areas where bruits are heard are the lumbar region in renal artery stenosis, iliac region in pregnancy (uterine artery) and over vascular tumors and malformations. The sites of auscultation for bruit in the addomen are given in Table 6.15; causes of hepatic bruit are given in Table 6.16.

Venous Hum

This is a continuous sound produced by increased venous flow. This is usually heard between the xiphisternum and the umbilicus due to turbulence of blood flow in well developed collaterals as the result of portal hypertension. This is known as Cruveilhier-Baumgarten syndrome. It is caused by a congenital patent umbilical vein draining into the portal vein.

Table 6.15: Sources of arterial bruits

• Celiac and mesenteric arteries-midline in the epigastrium
• Renal arteries—2.5 centimeters above and lateral to the umbilicus
• Iliac arteries—over the iliac fossae
• Hepatic bruit—over the liver

Table 6.16: Causes of arterial bruit over the abdomen

Bruit over the liver is heard in:
1. Hepatocellular carcinoma
2. Acute alcoholic hepatitis
3. Hepatic artery aneurysm
4. Hepatic A-V fistula

Table 6.17: Causes of splenic rub

Splenic rub may be heard in:
• Chronic myeloid leukemia
• Infective endocarditis
• Sickle cell anemia
• After splenic puncture

Table 6.18: Causes of hepatic rub

Hepatic rub is heard in:
• Hepatocellular carcinoma
• Infarction of liver (sickle cell anemia, polyarteritis nodosa)
• Hematoma around puncture site and after liver biopsy and liver abscess

Friction Rub

Rubs are produced by friction between inflamed visceral and parietal peritoneum during movement with respiration. The rub is heard in perisplenitis or perihepatitis caused by micro infarction and inflammation (Tables 6.17 and 6.18).

EXAMINATION OF THE GENITALIA

Examine the testes, penis, epididymis and spermatic cord in males by inspection and palpation. Retract the prepuce and examine the glans, corona glandis, shaft of the penis, root of the penis and urethra. Gently squeeze the penis to bring out any urethral discharge, which may be present in urethritis which is common in non-specific urethritis (NSU) and gonorrhea.If secretions are present, send them for gram staining, microscopy for gonococcus and for microbiological culture.

The testis is palpated individually. In children it is soft, in adults it is firm 2 to 2.5 cm in length. Gentle pressure elicits a sickening sensation known as testicular sensation. Hard enlarged testis with loss of testicular sensation suggests tumors commonly seminomas. A very common cause of scrotal enlargement is hydrocele, which is a frequent finding in lymphatic filariasis caused by collection of fluid in the tunica vaginalis around the testes as a result of lymphatic obstruction.

Anus and Rectum

The left lateral position is best for routine examination of rectum. Stand behind the patient's back, facing his feet.

Inspection

Separate the buttocks carefully and inspect the perianal area and anus. Note for any abnormality in the skin, skin tags, warts, fistula, fissure, sinuses, piles or prolapse.

Palpation (Digital Examination) (Fig. 6.12)

Palpation is done with index finger of right hand. Place pulp of the finger flat on the anus and press firmly and slowly in a slightly backwards direction. After initial resistance, the anal sphincter relaxes and the finger can be passed into the canal. Feel for any thickening or growth. Assess the prostate gland in males and cervix, uterus and ovarian lesions in females. On withdrawing the finger after examination look at it for evidence of mucus, pus and blood. Microscopy of the material on the finger may help to detect cellular exudates ova of worms and protozoa such as amoeba, giardia and balantidium. Normally palpitation of prostate may produce a sickening sensation at times, but pain and tenderness are abnormal.

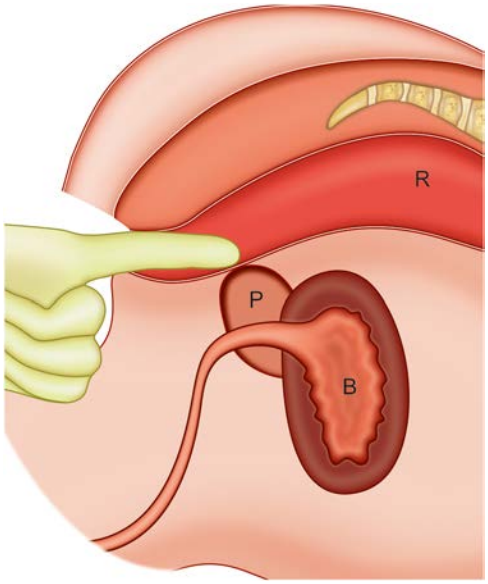


Fig. 6.12: Digital examination of rectum (R– rectum; P–prostate; B–urinary bladders)

APPENDIX-1

Clinical Points to Identify Abdominal Masses

	Liver	*Gallbladder*	*Spleen*	*Right kidney*	*Left kidney*	*Intestinal loops*	*Cecum and appendix*	*Lymph nodes*	*Uterus*	*Tubo-ovarian masses*	*Urinary bladder*	*Pancreas*
Site	Right hypo-chon-drium and epi-gastrium	Medial aspect of right hypochon-drium	Left hypo-chondrium	Right lumbar	Left lumbar	Any where usually umbilical, lumbar or iliac	Right iliac fossa	Along midline and iliac region	Rises up from hypogas-trium	Iliac fossae	Hypogas-trium	Umbilical, epigastrium
Move-ment with respiration	Free	Free	Free	Restr-icted	Restr-icted	Variable	Nil	Nil	Nil	Nil	Nil	Nil
Mobility	Nil	Mobile	Vari-able	Nil	Nil	Mobile	Vari-able	Vari-able	Lateral mobility	Vari-able	Nil	Nil
Borders	Sharp edge	Rounded	Sharp anterior border	Rounded	Rounded	Border not sharp	Rounded	Rounded	Rounded	Not sharp	Indistinct	Rounded
Percussion note	Dull	Dull	Dull	Band of resonance	Band of resonance	Resonant	Variable	Dull	Dull	Dull	Dull	Dull
Special points	Dull-ness continuous with normal liver dullness	Murphy's sign	Better felt in right lateral position	Palpable bimanu-ally	Palpable bimanually Insinuation of fingers above the mass possible	-	-	-	Auscultа-tion, pelvic examina-tion	Pelvic exami nation	Disappears on micturi-tion or cathete-rization	

APPENDIX-2

Common Causes of Enlargement of Abdominal Organs

Hepatomegaly

1. Tenderness present: Congestive cardiac failure, hepatic amoebiasis, liver abscess, biliary tract infections, viral hepatitis, alcoholic hepatitis.
2. Tenderness absent: Early stages of cirrhosis of liver, cysts hepatic tumors (primary and secondary), infiltrations, e.g. fatty change, hemochromatosis glycogen storage disease
3. As part of hepatosplenomegaly.

Splenomegaly

1. Mild (Less than 5 cm palpable) and moderate (up to 10 cm palpable): Acute infections, e.g. malaria, leishmaniasis, enteric fevers, infective endocarditis, viral hepatitis, septicemia and others, miliary tuberculosis, infectious mononucleosis, early stages of portal hypertension, leukemias, lymphomas, sickle cell disease, autoimmune hemolytic anemia, polycythemia vera.
2. Massive splenomegaly (10 cm and above): Portal hypertension, chronic myeloid leukemia, myelofibrosis, chronic malaria and leishmaniasis, other parasitic infections, thalassemias, cysts and tumors of the spleen, tropical splenomegaly.

Hepatosplenomegaly

Liver and spleen are enlarged to varying degrees.

Early stages of cirrhosis, leukemias, lymphomas, malaria, leishmaniasis, other parasitic infections, miliary tuberculosis.

Enlargement of the Kidneys

Tumors, hydro-and pyo-nephrosis, polycystic kidneys.

Enlarged Adrenals

Tumors

Lymph Nodes

Lymphomas, secondary deposits

Uterus and adnexa: Pregnancy, fibroids, ovarian cysts, ovarian tumors

Midline Masses

Advanced carcinoma of stomach with secondary nodes, pancreatic tumors and cysts, aortic aneurysm, retroperitoneal masses.

CHAPTER

7 Investigations in Gastrointestinal Disorders

KR Vinaya Kumar

Examination of feces, Examination of vomitus, Ascitic fluid analysis, Radiology of GI tract, Ultrasound scanning, Computed tomography, Magnetic resonance imaging, Gastrointestinal endoscopy, Manometry, Radioisotope studies, *Helicobacter pylori*, Gastric secretory studies, Tests used in pancreatic diseases, Studies for malabsorption states, Tumor markers, Fine needle aspiration cytology, Laparoscopy

EXAMINATION OF FECES

Detailed stool examination is the first step in many gastrointestinal (GI) diseases such as diarrhea, malabsorption, unexplained anemia and weight loss. The quantity, color, physical characteristics, presence of blood, leucocytes and parasites require special attention.

The amount may be copious or scanty, hard, formed, semiformed or liquid. Black color may be produced by altered blood or ingestion of iron or bismuth. Pallor of the stool as seen in obstructive jaundice may be due to lack of entry of bile into the intestine, dilution and rapid passage of stool through the intestine as in diarrhea or abnormally high fat content as in malabsorption. Silvery stools occur if there is a combination of obstructive jaundice with upper GI bleeding. In jaundice, the stools are very offensive.

Watery stools may occur in profuse diarrhea and after the administration of purgatives. In cholera, rice water stools may be passed. This contains very little organic matter and is almost odorless. Pus containing stools will be seen in severe dysentery and ulcerative colitis. Here there may be different amounts of blood as well. Slimy stools are found in large bowel disease due to presence of an excess of mucus. In intussusception, bloody stools occur which, look like red currant jelly. In brisk upper GI bleeding, the fresh blood may reach the rectum due to intestinal hurry and be passed in stools or as fresh blood itself. Stool in steatorrhea is large in quantity, pale, putty or porridge like and sometimes frothy with visible oily film. It often floats in water (especially in the closet).

Tests for Fecal Occult Blood

The *guaiac test* (hemoccult) is the most widely used for detecting occult blood. A filter paper impregnated with guaiac turns blue in the presence of hemoglobin when hydrogen peroxide is added. The test depends on the oxidation of guaiac in the presence of hemoglobin. False positive guaiac is seen with substances such as bananas, pineapple, broccoli and radish. False negative guaiac seen with ascorbic acid. The test is sensitive to a fecal blood loss of about 20 mL per day (Table 7.1).

Orthotoluidine test: 0.5 g of feces is mixed with 5 ml of distilled water and boiled. Around 0.25 ml

Table 7.1: Performance of the slide guaiac test for fecal occult blood

1. For 3 days before and during testing, patients should avoid the following: • Red meat, peroxidase-containing vegetables and fruits (e.g. broccoli, turnip, cantaloupe, cauliflower, radish) • Certain medications (e.g. iron supplements, vitamin C, aspirin and other NSAIDs)
2. Two samples of each of three consecutive stools should be tested. (It is proper to sample areas of obvious blood.)
3. Slides should be developed within 4–6 days. Slides should not be rehydrated prior to developing.

of fecal suspension is added to 1ml of orthotoluidine solution in glacial acetic acid. 0.25 ml of hydrogen peroxide is added to this mixture. A dark green color which develops within 3 minutes indicates positive reaction for occult blood.

Causes for False-Positive Tests

Exogenous Peroxidase Activity

- Red meat (nonhuman hemoglobin)
- Uncooked fruits and vegetables (vegetable peroxidase)
- Any other source of GI blood loss (e.g. epistaxis, gingival bleeding, upper GI tract pathology, hemorrhoids)
- Medications: Iron, vitamin C, NSAIDs.

Causes for False-Negative Tests

Storage of Slides

- Degradation of hemoglobin by colonic bacteria
- Ascorbic acid (vitamin C) ingestion
- Improper sampling/developing
- Lesion not bleeding at time of stool collection.

Other Tests for GI Blood Loss

1. Rapid testing using hematest tablets or hemastix
2. Spectroscopic methods
3. Isotopic methods using radioactive chromium labeled red cells.

Tests for Fecal Fat

Normal persons do not lose more than 6 g of fat thorough feces in 24 hours even when taking diets containing 100 g or more of fat. For estimation of fecal fat, the whole feces should be collected for 3 days when the patient is taking at least 50 g of fat daily orally. Estimation is done by titrimetric method of *Van de Kamer*. A semi-quantitative estimation of stool fat in a random sample can be done with Sudan stain. Fecal fat testing has largely been replaced by fecal elastase.

Stool Microscopy

First observe for motile parasites, e.g. vegetative forms of ameba, *Giardia lamblia* and *Strongyloides stercoralis*. Pathogenic ameba such as *E. histolytica* should be differentiated from nonpathogenic ameba such as *Entamoeba coli* (Figs 7.1 to 7.7).

Ova of various helminths are demonstrable by microscopy. If ova are scanty, concentration methods such as zinc sulphate floatation are employed.

Presence of fat globules and muscle fibers in feces indicate malabsorption states. Charcot-Leyden crystals are seen in chronic ulcerative lesions of intestine such as chronic dysentery and ulcerative colitis.

EXAMINATION OF VOMITUS

Examination of whole of the vomitus is important. Carefully look for the presence of blood (hematemesis), bile (bilious vomiting), parasites like round worms, food particles and toxic substances like drugs and poisons. Vomitus containing undigested food materials taken 4 to 6 hrs previously indicates

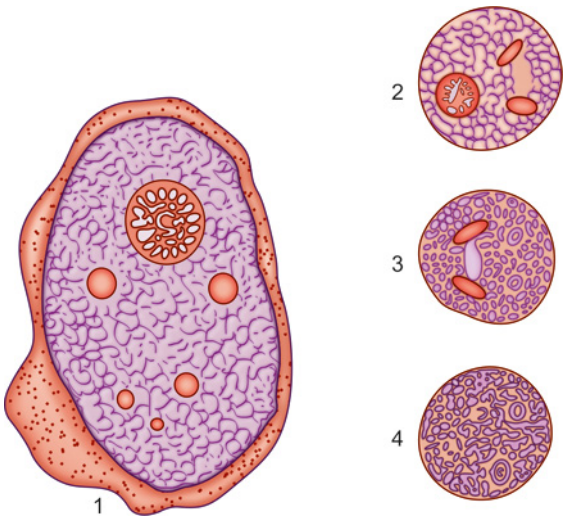


Fig. 7.1: *Entamoeba histolytica*. (1) Trophozoite (Vegetative motile form) with ingested erythrocytes (2) Uni and binucleated cysts with (3) Chromatoid bars and glycogen vacuole (4) Mature cyst with four nuclei

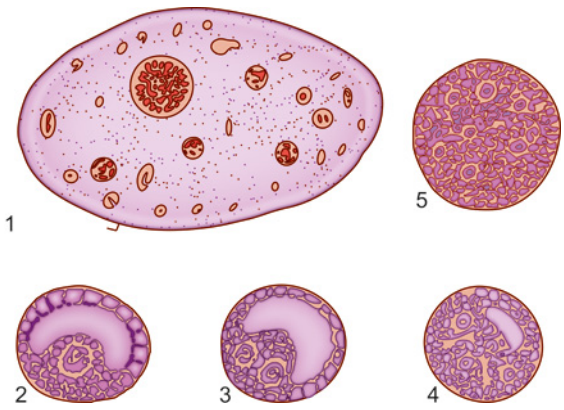


Fig. 7.2: *Entamoeba coli* in stools. (1) Trophozoite, (2–4) Uni, bi and quadrinucleate cysts with glycogen vacuole and chromidial bars. (5) Mature cyst with eight nuclei

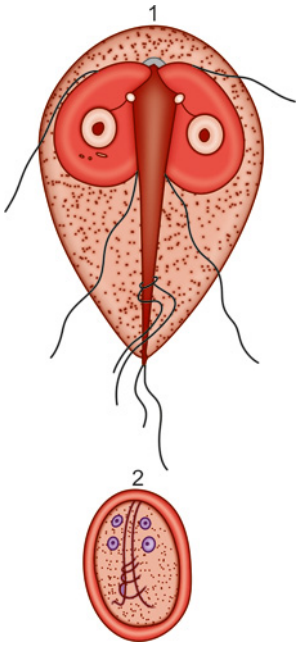


Fig. 7.3: *Giardia lamblia* in stools. (1) Trophozoite—note the suckers and flagella, and (2) Cyst

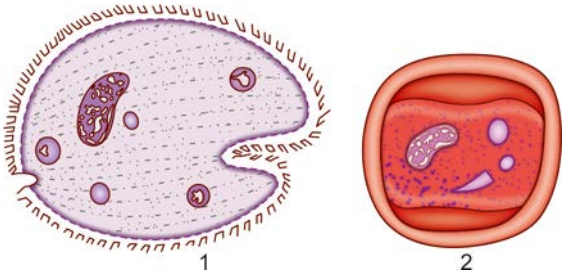


Fig. 7.4: *Balantidium coli*—in stools. (1) Trophozoite-motile ciliate, and (2) Cyst

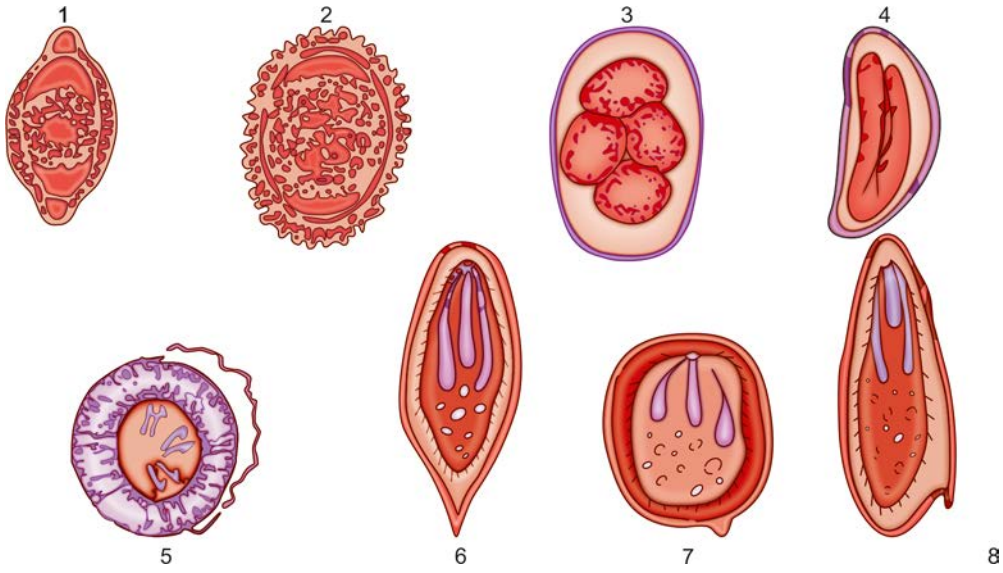


Fig. 7.5: Ova in stools. (1) *Trichuris trichiura*, (2) *Ascaris lumbricoides*—embryonated egg, (3) Hookworms, (4) *Enterobius vermicularis*, (5) *Taenia* (tapeworm), (6) *Schistosoma hematobium*, (7) *Schistosoma japonicum*, and (8) *Schistosoma mansoni*

gastric outlet obstruction or gastroparesis. Altered blood in the vomitus gives rise to coffee ground appearance. If there is any doubt, presence of blood should be confirmed by chemical examination. Fecal odor of the vomitus indicates gastrocolic fistula or hind gut obstruction. A sample of the vomitus should be sent for chemical examination for toxic substances and drugs when poisoning is suspected. It is important for medicolegal purposes.

ASCITIC FLUID ANALYSIS

Aspiration of peritoneal fluid is undertaken for diagnostic and therapeutic purposes. Site of aspiration is preferably two finger breadth



Fig. 7.6: *Strongyloides stercoralis* active larva in stool (× 100) arrow



Fig. 7.7: Adult whipworms with anterior end stuck into the colonic mucosa seen on colonoscopy

cephalad and two finger breadth medial to anterior superior iliac spine in the left lower quadrant. However, it can also be done in the midline below the umbilicus or in the right iliac fossa. In a patient with multiple abdominal scars, ultrasound guidance aspiration may be safer (Fig. 7.8). The fluid aspirated should be subjected to the following tests (Tables 7.2 to 7.4).

Gross Appearance of Ascitic Fluid

It may be watery when the protein concentration is low. It is transparent and slight yellow in transudates with low cellular content. Cloudy appearance is caused by neutrophils in ascitic fluid.

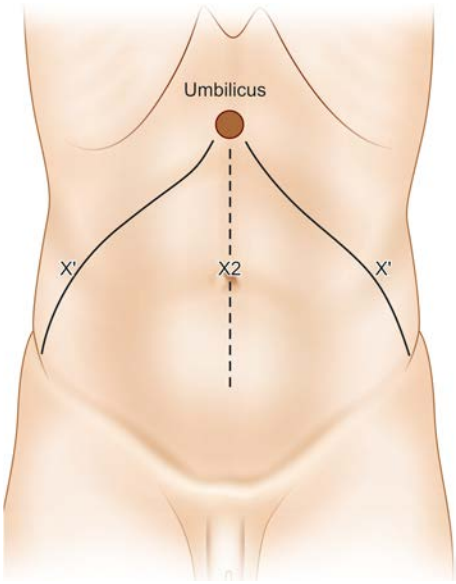


Fig. 7.8: Sites for aspiration of ascitic fluid

Blood stained fluid is found in hepatocellular carcinoma, peritoneal carcinomatosis, acute pancreatitis, tuberculosis and in traumatic tap. White or chylous ascites is caused when the lipid content (mainly triglycerides) exceed 200 mg/dl When the bilirubin content is greater than that of serum, the ascitic fluid is dark brown in color and this suggest biliary perforation. Secondaries from malignant melanoma make the ascitic fluid black (Tables 7.2 to 7.4).

The diagnosis of ***Spontaneous bacterial peritonitis (SBP)*** is made when there is a positive ascitic fluid culture and an elevated ascitic fluid absolute PMN count (i.e. at least 250 cells/mm^3 (0.25×10^9/L) without evidence of an intra-abdominal surgically treatable source of infection.

Table 7.2: Other biochemical and microbiological tests

Routine	*Optional*	*Required in special situations*
Cell count	Culture in blood culture bottles	TB smear and culture
Albumin	Glucose	Cytology
Total protein	LDH Amylase Gram stain	Triglyceride Bilirubin

Table 7.3: Classification of ascitic fluid infections

- Spontaneous bacterial peritonitis
- Monomicrobial non-neutrocytic bacterial ascites
- Culture-negative neutrocytic ascites
- Secondary bacterial peritonitis
- Polymicrobial bacterial ascites (needle perforation of the bowel)

The criteria for a diagnosis of ***Monomicrobial nonneutrocytic bacterial ascites (MNB)*** include:

1. A positive ascitic fluid culture for a single organism
2. An ascitic fluid polymorphonuclear (PMN) count lower than 250 cells/mm^3 (0.25×10^9/L)
3. No evidence of an intra-abdominal surgically treatable source of infection.

Culture-negative neutrocytic ascites (CNNA) is diagnosed when:

1. The ascitic fluid culture grows no bacteria
2. The ascitic fluid neutrophil count is > 250 cells/mm^3 (0.25×10^9/L)
3. No antibiotics have been given (not even a single dose), and
4. No other explanation for an elevated ascitic fluid neutrophil count (e.g. hemorrhage into ascites, peritoneal carcinomatosis, tuberculosis, or pancreatitis).

Secondary bacterial peritonitis is diagnosed when:

1. The ascitic fluid culture is positive (usually for multiple organisms)
2. The neutrophil count is 250 cells/mm^3 (0.25×10^9/L) or greater, and
3. An intra-abdominal surgically treatable primary source of infection, such as perforated gut or perinephric abscess is present.

Polymicrobial bacterial ascites is diagnosed when:

1. Multiple organisms are seen on Gram stain or cultured from the ascitic fluid and
2. The neutrophil count is lower than 250 cells/mm^3 (0.25×10^9/L). This diagnosis should be suspected when the paracentesis is traumatic or unusually difficult because of ileus, or when stool or air is aspirated into the paracentesis syringe. Polymicrobial bacterascites is essentially diagnostic of gut perforation by the paracentesis needle.

Serum-Ascites-Albumin Gradient

This is the difference between serum albumin and ascitic fluid albumin. This gradient is calculated by subtraction and is not a ratio. Unless a laboratory error has been made, the serum albumin concentration is always the larger value. This is based on oncotic-hydrostatic balance. If the Serum-Ascites-Albumin Gradient (SAAG) is 1.1 or greater, the patient can be considered to have portal hypertension with an accuracy of approximately 97% (Table 7.4).

Table 7.4: Classification of ascites by serum-ascites-albumin gradient

High Gradient ≥ 1.1 g/dL (11 g/L)	*Low Gradient <1.1 g/dL (11 g/L)*
Cirrhosis	Peritoneal carcinomatosis
Alcoholic hepatitis	Tuberculous peritonitis
Cardiac ascites	Pancreatic ascites
Mixed ascites	Bowel obstruction or infarction
Massive liver metastases	Biliary ascites
Fulminant hepatic failure	Nephrotic syndrome
Budd-Chiari syndrome	Postoperative lymphatic leak
Portal vein thrombosis	Serositis in connective tissue diseases
Sinusoidal obstruction syndrome	
Myxedema	
Fatty liver of pregnancy	

RADIOLOGY OF GI TRACT

Plain Radiograph

Radiological evaluation starts with plain films of the whole abdomen taken in the supine, upright and lateral positions. Soft tissues like liver, spleen, kidneys and fetal parts and bones will be seen. It also reveals radiopaque calculi of pancreas, biliary tree and urinary tract. Other radiological opacities include foreign bodies, calcified lymph nodes, phleboliths and calcification along the aorta and its branches. In bowel obstruction and paralytic ileus, gas and multiple fluid levels are seen. In bowel perforation, gas is seen under the diaphragm in an erect picture.

Jejunum is identified by the presence of volvuli conniventes, and colon by its haustrations. Distended small intestine presents a 'ladder pattern', i.e. dilated air filled loops are seen across the abdomen in the central part around the umbilicus. Distention of the large intestine produces 'the garland pattern', i.e. distended air-filled colon is seen occupying the periphery of the abdomen. Presence of free air in the biliary tract, or the layers of the intestinal wall can be identified in a good film taken with suitable preparation.

Indications for Plain Radiograph of Abdomen

1. Acute abdominal emergencies
2. To delineate radiopaque calculi
3. To detect organomegaly.

Contraindication for taking X-ray abdomen: Viable pregnancy.

Contrast Radiography

X-ray contrast studies are indicated in the following conditions:

1. To demonstrate anatomical abnormalities such as change in shape and size of hollow viscera, ulcers, new growths, fistulae, strictures, diverticulae, blind loops, intrinsic or extrinsic compression of normal viscera and the like.
2. To study abnormalities in motility of the gut: Passage of the contrast material can be followed up by serial radiographs, or on the fluorescent screen. This will reveal abnormalities of gut motility as in corkscrew esophagus and congenital megacolon, obstruction to flow as in pyloric stenosis and diagnostic changes in intestinal hurry, malabsorption states and so on (Figs 7.9 to 7.12).

Contrast Studies

These are done with barium sulphate or iodinated compounds given orally or as enema. Barium sulphate is the commonly used agent since it is inert, non-toxic, cheap and easily available. It coats the mucosal surface of the gut. The aqueous iodinated agents include Gastrografin (diatrizoate meglumine and diatrizoate sodium) and Hypaque (diatrizoate sodium). Unlike barium sulphate which has to be given in large quantities and which is unpalatable, the iodinated compounds are more pleasant to take. Moreover, they are less irritant even when introduced into the peritoneum or body cavities. Therefore, their main indications are in suspected perforation of esophagus, perforated duodenal ulcer, leaks from surgical anastomosis and acute diverticulitis.

Esophagus

Barium swallow forms the initial investigation in esophageal evaluation. High density thick barium paste is swallowed and pictures are taken as the contrast material fills the lumen and coats the mucosal surface. These demonstrate anatomical abnormalities and motility disorders (Fig. 7.9).

Malignancy of the esophagus is seen as an irregular filling defect and distal obstruction. The proximal dilatation is mild due to infiltration of the esophageal wall and this contrast with the gross dilatation seen in achalasia cardia. In extrinsic compression, the indentation of the barium filled esophagus is smooth and the mucosa is not ulcerated. Esophageal varices stand out as linear filling defects in the lower third. In achalasia cardia, the esophagus is grossly dilated and the lower portion tapers smoothly (pencil beaking). In dysphagia, i.e. dysphagia produced by aberrant



Fig. 7.9: Achalasia cardia barium swallow. Note dilated esophagus above. Smooth narrowing of lower part (arrow)



Fig. 7.10: Barium swallow corkscrew esophagus (due to spasm)

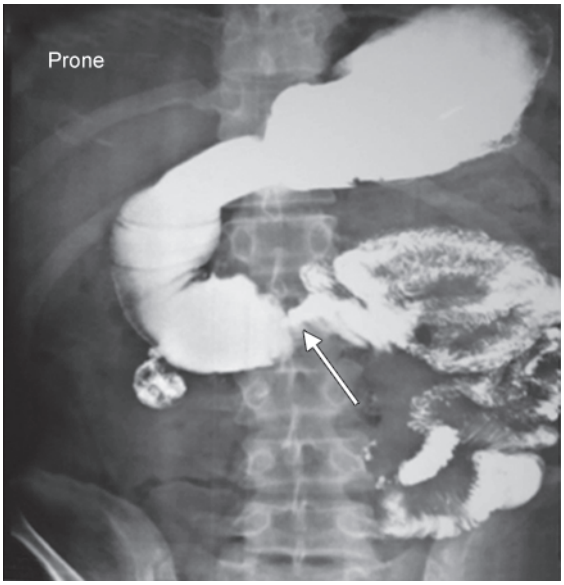


Fig. 7.11: Barium meal showing narrowing of duodenal lumen by adenocarcinoma (arrow)

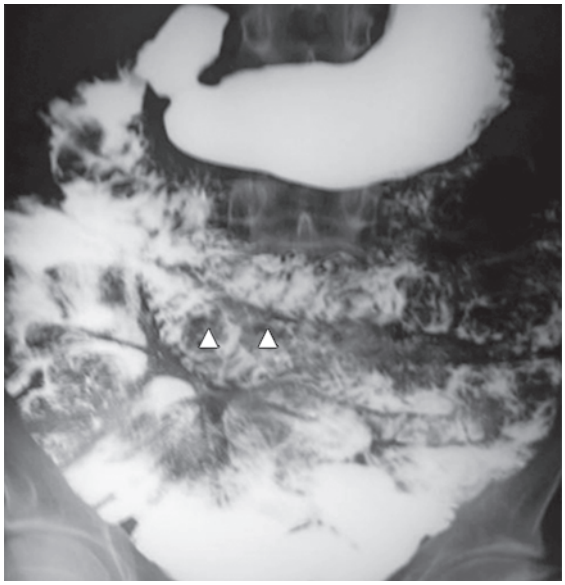


Fig. 7.12: Barium meal follow-through showing polyposis in the small intestine. *Note:* Filling defects caused by the polyps (arrowheads)

blood vessels, compression is usually at the upper level.

Diffuse esophageal spasm gives the appearance of cork screw esophagus (Fig. 7.10). Double contrast study (barium and air) clearly shows lesions of esophagitis. In peptic esophagitis, lesions are seen in the lower part. Monilial esophagitis gives the picture of small, multiple intramural diverticuli.

Stomach and Small Intestine

These are visualized by *barium meal examination.* 500 to 600 ml of thin suspension of barium sulphate is drunk within 5 minutes and films taken at regular intervals to follow the progress of the barium.

Usually the pictures are taken at 5 minutes, 30 minutes, 1 hour, 3 hours and 12 to 24 hours. Normally the stomach and duodenal cap are well seen in the 5-minute picture. By 30 minutes, part of the barium would have entered the duodenum and small intestine which are visible. The stomach is empty in 2½ to 3 hrs and the head of the meal reaches the ileocecal region and enters the ascending colon by this time. The whole meal is seen in the descending and sigmoid colon by 16 to 24 hours. Delay in the progress of the meal and unusual hurry are both indicative of disease (Figs 7.11 and 7.12).

Double Contrast Technique

Conventional barium meal may detect only 50% of lesions in the stomach. The diagnostic yield can be improved to 90% by double contrast barium study. A small quantity of special high density barium is used which coats the mucosal wall. The stomach is distended with air which forms a good contrast. This is achieved by swallowing effervescent tablets. The patient is tilted so as to shift the barium in the stomach and to study the barium coated mucosa.

In many cases, benign gastric ulcer can be distinguished from carcinoma. Erosive gastritis is seen only in double contrast studies and are seen as small linear collections of barium.

Radiological diagnosis of duodenal ulcer is based on direct and indirect evidences. The direct evidence is the ulcer crater. Indirect evidences include deformity of the duodenal cap, pseudo-diverticuli, spasm and evidence of gastric outlet obstruction. Ninety percent of duodenal ulcers are seen in the first part of duodenum. Anastomotic ulcers are not seen well in the barium films.

Small Intestine

Conventional barium meal study will not give adequate information about the small intestine since the barium gets diluted.

Enteroclysis (small bowel enema) is a technique by which a tube is passed into jejunum under fluoroscopy and barium is given through the tube directly into the jejunum. Small intestinal dilatation (more than 3 cm in diameter) is seen in mechanical and dynamic obstructions, diabetes, hypercalcemia, postvagotomy state and in sprue. The mucosal folds are thickened (more than 3 mm) in giardiasis, strongyloidosis, lymphoma, Zollinger-Ellison syndrome, hypoproteinemia and rare diseases like Whipple disease. Submucosal lesions are seen as thumb impressions and are observed in submucosal hemorrhage, lymphoma, Crohn's disease and amyloidosis. Intestinal loops are tethered together in conditions such as radiation enteritis, tuberculosis and Crohn's disease (desmoplastic effect). Small intestinal fistulae and ulcerations are better visualized by enteroclysis. One of the common causes of ileal ulceration and stenosis in India is intestinal tuberculosis. In this condition, there are radiological abnormalities of the cecum consisting of ulceration, distortion and damage to ileocecal valve. Pulled up cecum, and congenital abnormalities of rotation of the gut can also be made out in barium meal follow-through. Polyps and benign tumors may appear as filling defects (Fig. 7.12).

Large Intestine

It is visualized by barium enema. For getting best results one should ensure that the patient had a full bowel movement on the morning of the test. In constipated individuals, the colon can be washed out with saline using a flatus tube. A thin suspension of barium sulphate is prepared and administered as enema. The progress of the head of the barium and filling of the colon can be checked in the fluorescent screen. In the vast majority of subjects, the whole colon up to the terminal ileum can be visualized. Pictures are taken in the barium filled phase, post-evacuation phase and after insufflation of air into the rectum, for double contrast.

Contrast studies are usually done for suspected malignancy, polyps, ulcerative colitis, strictures, diverticulitis, congenital megacolon and obstruction. To make out the filling defects, strictures, fistulae and obstruction, single contrast is enough. Double contrast gives the mucosal details and is very helpful in the diagnosis of diverticulae, polyps, ulcerative colitis and the like. In ulcerative colitis, colon becomes shorter with loss of haustrations and the mucosa becomes granular. Fine mucosal ulcers can be seen. Later, pseudopolyps and strictures appear. Malignancy is often seen as filling defects-apple core deformity, or as strictures.

Selective Angiography

The celiac and mesenteric arteries or their branches can be selectively catheterized and contrast injected (Fig. 7.13).

Indications

a. For detecting the site and lesion in obscure GI bleeding such as angiodysplasia and hemangioma which can also be embolized.
b. For detecting functioning microtumors of pancreas which may be missed even in CT scan.
c. Preoperative assessment of vascularity and vascular feeders in hepatocellular carcinoma.
d. Chemo-embolization of nodules in hepatocellular carcinoma.
e. For locating vascular occlusion in ischemic bowel disease.

ULTRASOUND SCANNING

Ultrasound scan (USS) is a non-invasive diagnostic technique, extremely useful in evaluating the intra-

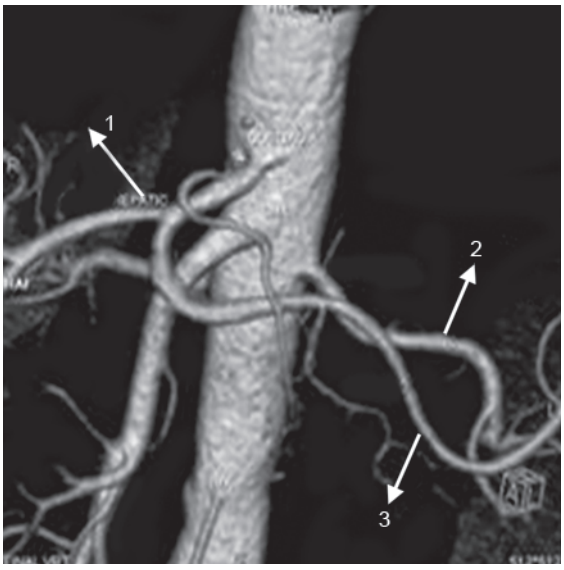


Fig. 7.13: Angiography (DSA) showing various branches of the aorta (1) Common hepatic artery, (2) Left renal artery, (3) Splenic artery

abdominal lesions, especially of the parenchymal organs. All the abdominal and pelvic organs can be well delineated by USS. With proper positioning of the probes all the solid and hollow organs can be imaged. The size, shape, consistency, movement and presence of pathological lesions can be accurately charted. The size of the lesions can be measured and documented and this will give immense help for following up the progress of the lesion. Pelvic structures can be better imaged by vaginal probes. Intervention procedures such as aspiration and biopsy can be done under ultrasound guidance with a higher degree of accuracy and safety. The yield of picking up of lesions can be enhanced and more accurately delineated by the use of doppler attached to USS especially for vascular lesions (Figs 7.14 to 7.16).

COMPUTED TOMOGRAPHY

Computed Tomography (CT) scan can demonstrate tumors, abscesses, fluid collections, lymph nodular masses and several other abnormalities in the abdomen. Details of parenchymal lesions of the liver, spleen, pancreas, kidneys, adrenals, lymph nodes, uterus and its adnexa can be made out clearly. The CT scan is superior to ultrasound scan for detecting pancreatic lesions, defining lymph node masses as in lymphoma, common bile duct stones, adrenal tumors and hepatic metastases. Hence it is very useful for assessing operability of intra-abdominal neoplasms and staging of lymphomas (Fig. 7.17).

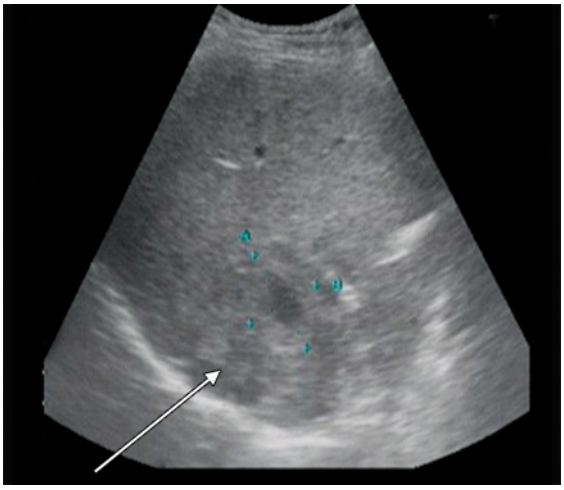


Fig. 7.14: Ultrasound scan showing liver focal lesion (arrow)

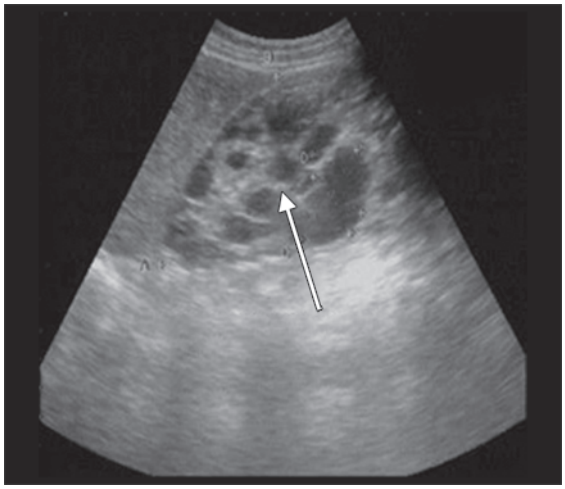


Fig. 7.16: Ultrasound scan showing polycystic kidney (arrow)

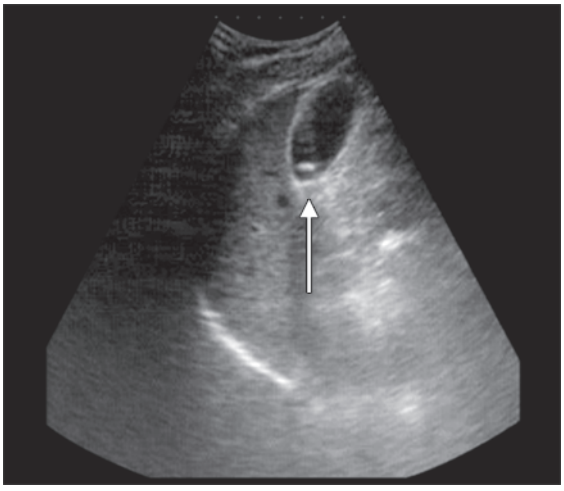


Fig. 7.15: Ultrasound scan showing gallbladder stone (arrow)

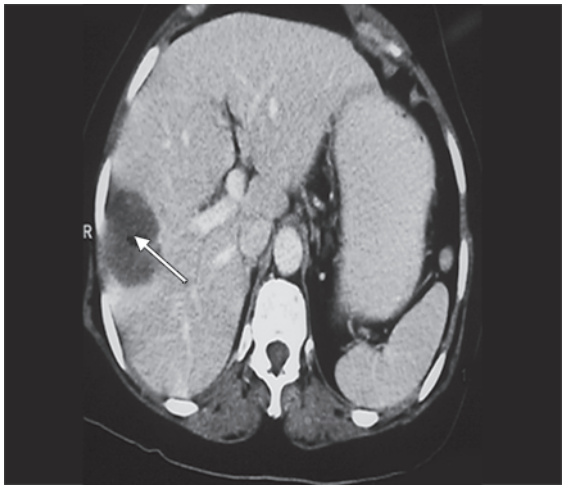


Fig. 7.17: CT scan showing focal hepatic lesion abscess (arrow)

Virtual Colonoscopy

Helical CT generates high resolution two dimensional images of abdomen and pelvis. From this data, the computer reconstructs three-dimensional images of colon. It is noninvasive and quick and does not require elaborate bowel preparation. For these reasons it is more acceptable to the patients, but their absolute reliability is not yet firmly established. The disadvantage is that interventions such as biopsy, polypectomy and other procedures cannot be performed simultaneously.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) scan is undertaken in special situations when it has specific advantages. These include clear distinction between different types of tissues and noninterference with bony structures. Specific studies of functions of tissues can be undertaken using special techniques along with MRI, e.g MRI spectroscopy and others (Figs 7.18 and 7.19).

Magnetic resonance cholangiopancreatography (MRCP) is a newer imaging technique to delineate bile duct and pancreatic duct systems. MRCP is very accurate and is fast replacing endoscopic retrograde cholangiopancreatography (ERCP) in some situations. It is noninvasive and cheaper compared to ERCP and does not involve radiation. The disadvantage is that interventions are not possible (Fig. 7.20).

GASTROINTESTINAL ENDOSCOPY

Direct endoscopy is the technique of direct visualization of the interior of hollow viscera in any part of the body using appropriate flexible instruments, fiberoptic light sources, operating channels, cameras or ultrasound instruments and special tools for imaging and intervention such as lithotomy, polypectomies, clipping or occluding blood vessels biopsy and even submucous resection of neoplasms and several other surgically amenable conditions. Endoscopies have developed and reached a state of near perfection at present. The findings within hollow viscera can be seen on the television screen, imaged digitally, stored and used for follow-up. GI endoscopy is available in several secondary and tertiary care hospitals in India at moderate costs

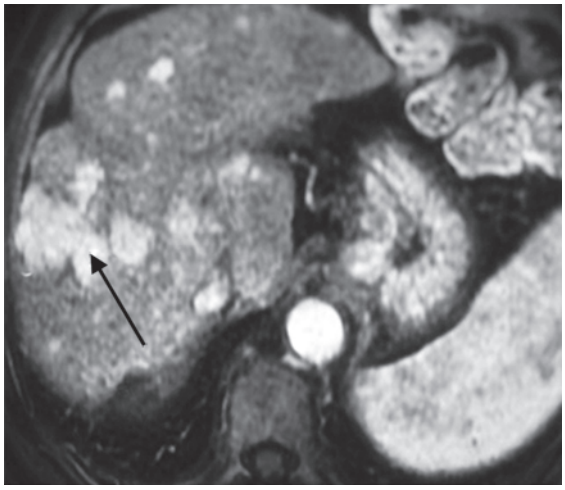


Fig. 7.18: MRI showing hepatocellular carcinoma (arrow)

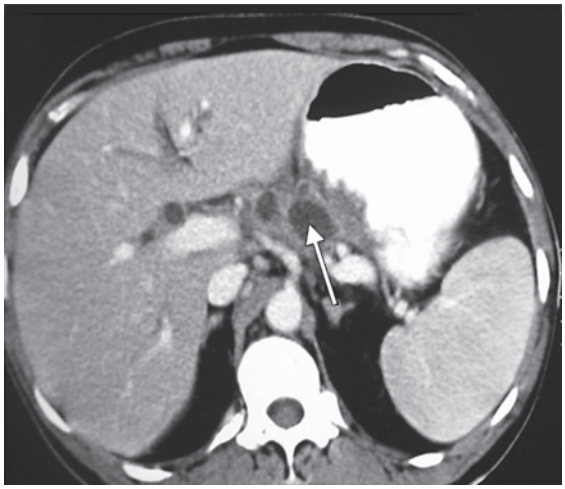


Fig. 7.19: MRI showing cysts in the pancreas (arrow)

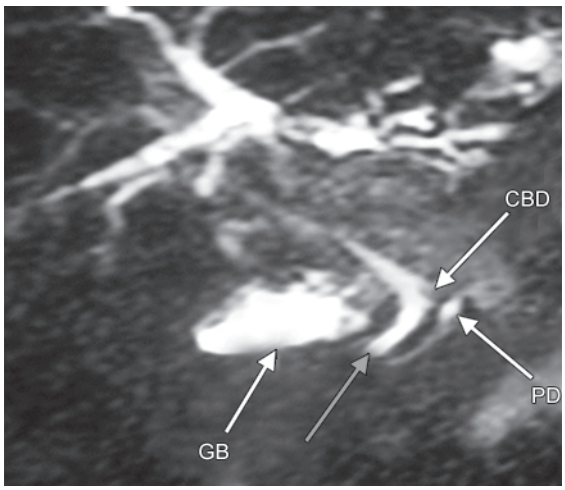


Fig. 7.20: Magnetic resonance cholangiopancreatography (MRCP) showing stricture (green arrow) of common bile duct (CBD). PD indicates panacreatic duct

(Rs 1000-5000). Endoscopic diagnosis with biopsy is the most reliable direct method to diagnose mucosal and submucosal lesions. This investigation should be done wherever possible if the diagnosis by indirect methods is still in doubt.

Upper GI Endoscopy (Esophagogastro-duodenoscopy—OGD scopy)

This is performed by passing a flexible endoscope through the mouth into the esophagus, stomach, bulb and second part of duodenum. The procedure is the best method for the examination of upper GI mucosa. OGD scopy is superior for the detection of gastric ulcers and flat mucosal lesions like Barrett's esophagus. It permits directed biopsy and endoscopic therapy, including foreign body retrieval (Figs 7.21 to 7.23).

Colonoscopy

Direct visualization of the colon by endoscopy using a colonoscope is colonoscopy. This technique has advanced to a high level of perfection so that in the hands of a expert *who is taking sufficient time to complete the investigation* all parts of the colon and even terminal ileum can be inspected and procedures undertaken.

Colonoscopsy is performed by passing a flexible colonoscope though the anal canal into the rectum and colon. It requires bowel preparation prior to the procedure. Cecum can be reached in more than 95% of the cases, and terminal ileum can also be examined. Colonoscopy is the gold standard for diagnosis of colonic mucosal disease. Colonoscopy has greater sensitivity than barium enema or CT scan for colitis, polyps and cancer. It permits directed biopsy, and other interventions (Figs 7.24 to 7.26). Helminths attached to colonic flora can be seen.

Flexible Sigmoidoscopy

It visualizes rectum and variable portion of left colon, typically upto 60 cm from the anal verge. Flexible sigmoidoscopy is primarily used for evaluation of diarrhea and rectal outlet bleeding. Mucosal lesions like ulcerative colitis, diverticulitis, carcinoma, polyps, strictures can be diagnosed with certainty.

Small Bowel Endoscopy

Three techniques are currently used to evaluate the small intestine:

1. *Push enteroscope:* It is performed with a long endoscope similar in design to an upper GI

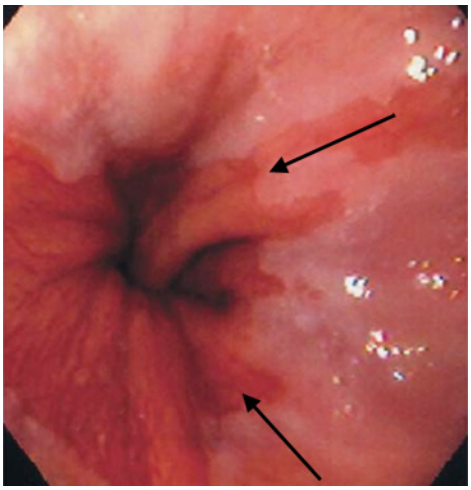


Fig. 7.21: Esophagoscopy showing Barrett's esophagus, i.e. squamous epithelium is replaced by intestinalized columar epithelium (arrows)

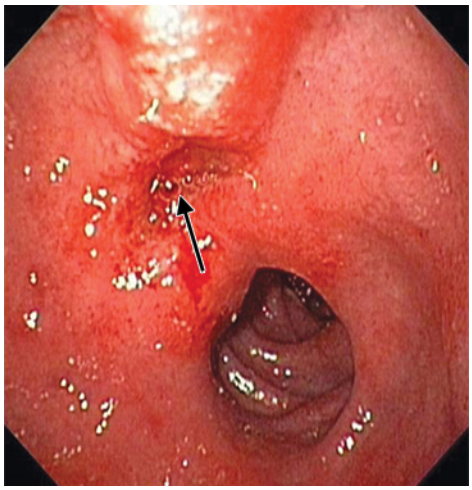


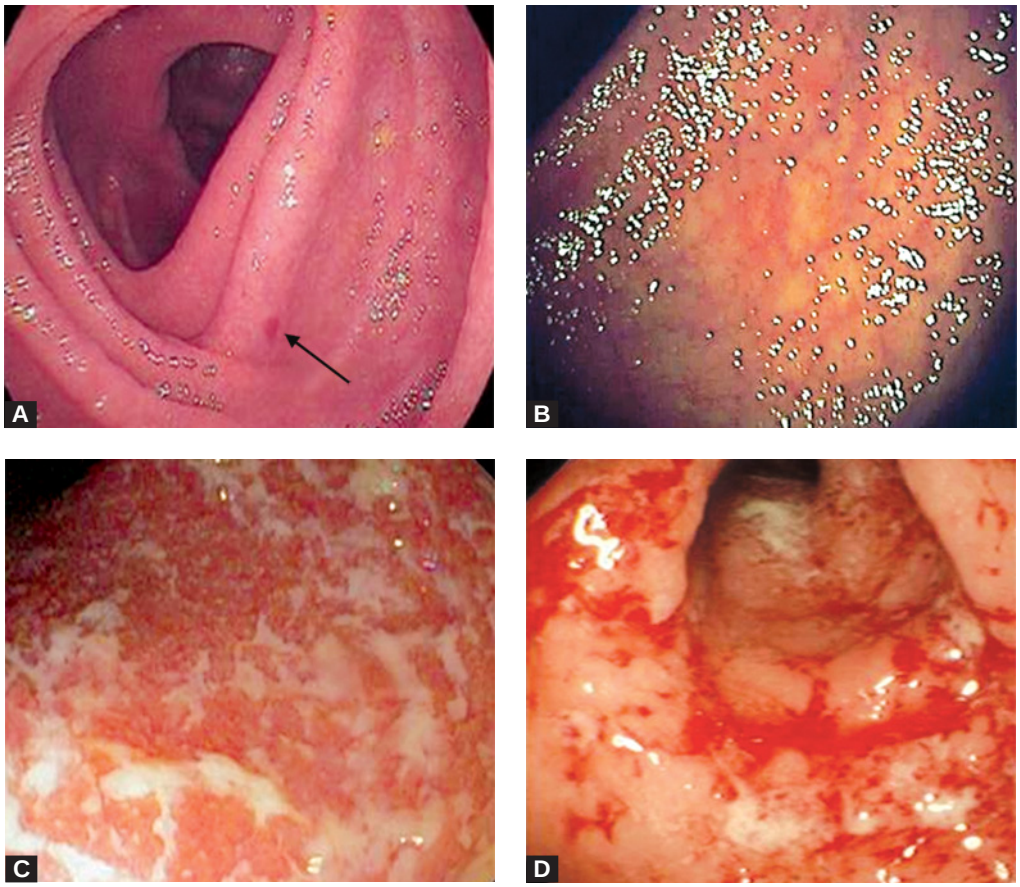
Fig. 7.22: Upper GI endoscopy showing bleeding gastric ulcer (arrow)



Fig. 7.23: Upper GI endoscopy showing carcinoma of the stomach with everted margins and bleeding (arrow)



Fig. 7.24: Colonoscopic appearance of tuberculosis



Figs 7.25A to D: Ulcerative colitis stage 1. (A) Note easy friability of the mucosa and tendency to bleed (arrow), (B) Progressive granularity and tendency to bleed, (C) Extension of ulcers and exudates, (D) Polypoid muscosa with ulceration and bleeding. These polypoid lesions are precancerous

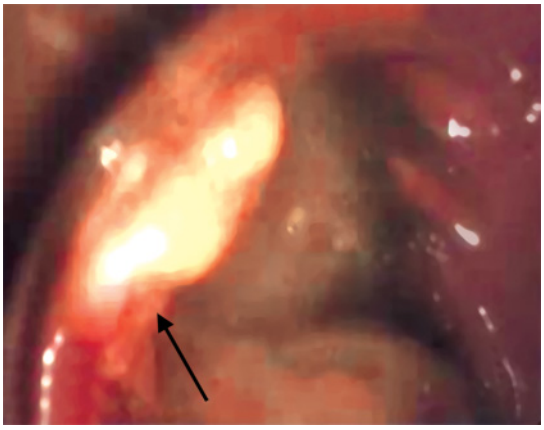


Fig. 7.26: Carcinoma colon. *Note:* Fungating growth (arrow)

endoscope. Enteroscope is pushed down into the small bowel, sometimes with the help of a stiffening overtube that extends from the mouth to the small intestine. The midjejunum is usually reached. The endoscope's instrument channel allows for biopsies or endoscopic therapy.

2. *Double balloon enteroscopy:* Here a long overtube and endoscope, both are equipped with balloons that when inflated appose the intestinal wall and allow for pleating of the small intestine over the endoscope and overtube. The double balloon enteroscope may be passed orally or anally.
3. *Capsule endoscopy:* The patient swallows a disposable capsule that contains a complementary metal oxide silicon (CMOS) with chip camera. Color still images are transmitted wirelessly to an external receiver at several frames per seconds until the capsule battery is exhausted or it is passed out in feces. This instrument can be used only once. It is expensive.

Endoscopic Retrograde Cholangiopancreatography

This is a combined endoscopic and radiological procedure to inspect the biliary and pancreatic duct system. A side viewing endoscope is passed into the second part of duodenum. The ampulla of Vater is identified and cannulated. The cannula can be directed into the common bile duct or pancreatic duct and contrast is injected. The picture is seen in the telescreen and spot films are taken. It reveals common bile duct stones, strictures, malignancy, pancreatitis and pancreatic pseudocysts. The pancreatic juice and bile can be aspirated through the cannula and subjected to further analysis and microbiological studies.

An advance in the field of endoscopy is the mother and babyscope. Through a side viewing endoscope a choledochoscope can be passed into the common bile duct. Similarly a babyscope can be passed into the terminal ileum through a colonoscope.

Interventions such as removal of stones and sphincterotomy can also be undertaken during endoscopic retrograde cholangiopancreatography (ERCP).

Endoscopic Ultrasound

This utilizes high frequency ultrasound transducers incorporated into the tip of a flexible endoscope. Endoscopic ultrasound (EUS) provides the most accurate preoperative local staging of esophageal, pancreatic and rectal malignancies. It is also highly sensitive for bile duct stones, gallbladder diseases, submucosal GI lesions and chronic pancreatitis.

MANOMETRY

Esophageal Manometry

Intraluminal manometry is important for diagnosing esophageal motor disorders such as achalasia cardia, reflux esophagitis, scleroderma and diffuse esophageal spasm. The pressure abnormalities in these conditions can be identified indirectly by positioning recording probes. Intraluminal manometer measures both the hydrodynamic pressure within the fluid bolus and the contact or squeezed pressure of the valve on the manometric probe (Fig. 7.27).

Video Manometry

This records simultaneous esophageal pressures with barium swallow.

Anorectal Manometry

Anorectal manometry measures the resting and active pressures generated by the sphincter complex of the anus. Resting pressure is contributed 85% by the internal anal sphincter and 15% by the external anal sphincter. Normal value is 40 to 80 mm Hg.

The test measures pressure gradients all along the anal canal both radially and longitudinally.

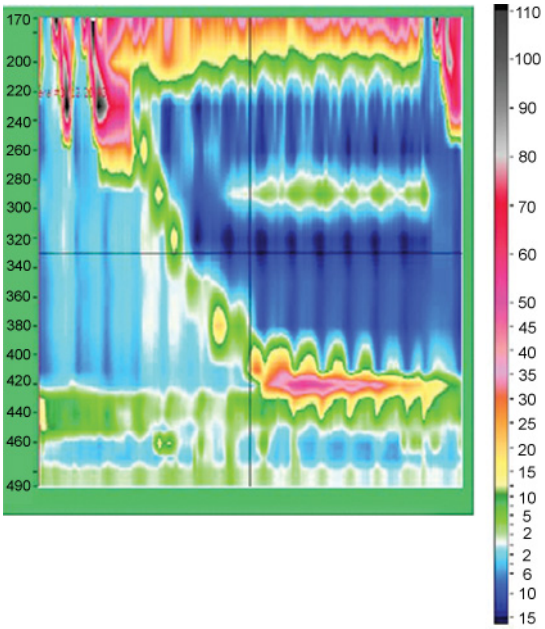


Fig. 7.27: Record of dynamic pressure changes by esophageal manometry in normal

Manometry also measures the minimum sensory volume (usually 10–15 ml)—determined by instilling volume into rectal balloon until sensed by urge to defecate.

Another parameter tested is Resting Anal Inhibitory Reflux (RAIR) which corresponds to decrease in resting pressure attributed to balloon distension in the high pressure zone, with an associated external anal sphincter contraction.

Indications of Manometry

1. Fecal incontinence
2. Constipation
3. Dyssynergic defecation
4. Hirschsprung's disease
5. Anal fissures.

Uses

1. Anorectal manometry can define hypo- or hyper-functional disorders of the sphincter mechanism.
2. Manometry can compare objective function with patient's subjective sensation of rectal fullness.
3. Often performed in conjunction with other diagnostic modalities like video defecography.

RADIOISOTOPE STUDIES

Radioisotope studies are used for the following indications:

1. Absorption of material from the intestinal tract can be studied using labeled substances e.g. fats, cyanocobalamin, etc. These tests are employed for the investigation of malabsorption states.
2. To study the rate of destruction of labeled erythrocytes in the spleen, in the diagnosis of hemolytic anemias, and to decide upon splenectomy as a therapeutic measure.
3. Isotope labeled erythrocytes to detect the site of gastrointestinal bleeding
4. Study of obstructive jaundice.
5. Use of labeled neutrophils to locate intra-abdominal abscesses.
6. Radioisotope of technetium or colloidal gold is useful in detecting primary or secondary hepatic tumors, abscesses and cysts by a gamma camera.

HELICOBACTER PYLORI (H. PYLORI)

H. pylori infection is well recognized to be causally related to duodenal and gastric ulcers, atrophic gastritis, gastric adenocarcinoma and gastric MALT lymphoma. Detection of *H.pylori* and eradication of this infection are important steps in the prevention and management of these disorders.

Tests commonly used to detect *H.pylori* are given in Table 7.5.

GASTRIC SECRETORY STUDIES

In the past, studies of the gastric aspirate were used extensively for the diagnosis of various diseases affecting the stomach. With the universal availability of direct methods such as endoscopy and biopsy, gastric acid estimation has become rare in clinical practice. Still, this test is done occasionally

Table 7.5: Tests to detect *H.pylori*

Test	*Sensitivity/specificity %*
Invasive (Endoscopy/Biopsy)	
Rapid urease	80-95/95-100
Histology	80-90/>95
Culture	-/-
Non-Invasive	
Serology	>80/>90
Urea breath test	>90/>90
Stool antigen	>90/>90

for the diagnosis of Zollinger-Ellison syndrome and for research purposes.

After an overnight fast for eight hours all the resting gastric juice is aspirated by continuous suction through a Ryle's tube. Basal acid output (BAO) is determined from the gastric juice sucked continuously for the next one hour. The normal value ranges from 54–80 mL of N/10 HCl/hr (or 10 mmoL/L).

After this a subcutaneous injection of histamine or pentagastrin in appropriate doses is given to stimulate gastric acid secretion maximally. The gastric juice is collected for the next one hour by continuous suction and hydrogen ion concentration is determined. Maximum secretion is 201 ± 53 mL/h in males and 153 ± 33 mL/h in females. The acid output is 3.7 ± 2.1 mEq/L in males and 2.2 ± 1.7 mEq/L in females. Patients with gastric ulcer and carcinoma have low outputs. On the other hand patients with duodenal ulcer and Zollinger-Ellison syndrome have raised values. If the ratio of BAO / MAO exceeds 0.6, it is highly suggestive of Zollinger-Ellison syndrome.

Measurement of serum gastrin must be made in the fasting state. Acid suppressing drugs should be avoided for a few weeks before the test. Blood is collected into special preservatives. In Zollinger-Ellison syndrome the level of gastrin in the serum is increased above 100 ng/L. Serum gastrin levels are also increased in renal failure, pernicious anemia, after vagotomy and during acid suppression therapy.

TESTS USED IN PANCREATIC DISEASES

Pancreatic Enzymes

Serum Amylase

Pancreatic inflammation leads to very high enzyme levels. Amylase levels can also be tested in urine, ascitic fluid and also in pleural fluid.

Serum Lipase

Elevation of pancreatic lipase is more specific for pancreatic inflammation.

Serum Trypsinogen

Elevated in acute pancreatitis. Decreased in chronic pancreatitis with steatorrhea Normal in chronic pancreatitis without steatorrhea and in steatorrhea with normal pancreatic function.

Pancreatic Enzyme Tests

1. *Secretin-Pancreozymin Test*: Secretin leads to increased output of pancreatic juice and bicarbonate. Cholecystokinin (CCK) leads to increased output of pancreatic enzymes. Pancreatic secretory response correlates with the functional mass of pancreatic tissue.
2. *Microscopic examination of stool for undigested meat fibers and fat*: Lack of proteolytic and lipolytic enzymes causes decreased digestion of meat fibers and triglycerides. Undigested muscle fibers and fat globules can be detected in feces.
3. *Determination of quantitative stool fat*: Lack of lipolytic enzymes brings about impaired fat digestion. Twenty four hour stool fat exceeds 7 g and neutral fats are present.
4. *Stool nitrogen*: Lack of proteolytic enzymes leads to impaired protein digestion, resulting in an increase in stool nitrogen.
5. *Measurement of fecal elastase*
6. *Dual labeled Schilling test*: Intrinsic factor cobalamin and Hog R protein cobalamin are given together. Urinary excretion of both types of cobalamin is determined and the ratio of different cobalamins is determined. Proteases are necessary to cleave R protein cobalamin. The ratio of labeled cobalamins gives an index of exocrine proteolytic function of the pancreas.

STUDIES FOR MALABSORPTION STATES

Intubation studies: Specially designed flexible tubes with modified ends are available to be introduced orally or nasally, so as to reach the stomach, small intestine or colon. The position of the tip can be checked by fluoroscopy. Samples of intestinal contents can be aspirated and examined for their nutrient content, state of digestion and microbial flora.

This helps to study the digestive and absorptive processes, and to identify the cause for malabsorption. Endoscopic biopsies have now replaced capsule biopsies of small intestine

Biopsy Studies

Reliable methods to get tissue under vision are endoscopic and laparoscopic biopsies. The specimen can be studied histologically, cytochemically, by immunofluorescence and by microbiological methods. Aspiration of intestinal contents and

biopsy studies are helpful in investigating cases of malabsorption, chronic diarrhea, intestinal obstruction, granulomatous disease and tumors.

Breath Analysis

When there is bacterial contamination in the small intestine, test substances like lactulose are degraded with the production of hydrogen or carbon dioxide which is absorbed and eliminated in expired air. Determination of hydrogen or carbon dioxide level in expired air gives clue to the presence of bacterial colonization of the small intestine, thereby revealing the cause of malabsorption.

D-Xylose Absorption Test

D-Xylose is absorbed passively from the ileum and excreted as such in urine. 5g of d-xylose is given orally dissolved in water. The urinary excretion over the next five hours is estimated. Normally 20% of the ingested xylose should be eliminated in urine, if renal function is normal. Estimation of plasma levels of d-xylose helps to confirm whether the xylose is getting absorbed. This test is abnormal in diseases affecting the ileum.

Lactose Tolerance Test

Lactose is digested by lactase, converted into glucose and absorbed. 50 g of lactose is given orally and the blood glucose is determined. In lactase deficiency, digestion of lactose is defective and so the blood glucose level does not come up. Lactase deficiency is a common cause of milk intolerance and diarrhea in children.

Serology

Antibodies such as IgA antiendomysial antibody, anti-tissue transglutaminase antibody, and antigliadin antibody are useful in the diagnosis of celiac sprue.

TUMOR MARKERS

Tumor marker assays are useful for the detection of malignancy, follow-up of response to treatment and early diagnosis of recurrence. The common tumor markers estimated in abdominal malignancies are:

a. Carcino embryonic antigen (CEA) in colon cancer.
b. Alpha fetoprotein (AFP) in hepatocellular carcinoma.
c. Human chorionic gonadotropin (HCG) in gonadal tumors and choriocarcinoma.
d. Acid phosphatase and prostate specific antigen (PSA) in prostatic enlargement—both benign and malignant.
e. CA 19-9 in pancreatic cancer.

FINE NEEDLE ASPIRATION CYTOLOGY

Fine needle aspiration cytology (FNAC) is a safe and simple office procedure, especially for the detection of cancer, where reliable result can be obtained within 30 minutes. The lesion is aspirated with a 5 to 10 mL syringe through a 24 to 26 G needle of suitable length. The aspirate is spread on a glass slide and is processed either by dry or by wet method and stained. The diagnostic yield can be improved by doing guided FNAC under ultrasound or CT scan control.

LAPAROSCOPY

Laparoscopy is an invasive diagnostic procedure in which the peritoneum is inspected directly through a laparoscope. The laparoscope is introduced through a small incision and a pneumoperitoneum is produced. Most of the viscera can be inspected directly and biopsies can be taken. The diagnostic yield is much higher than blind biopsies. Complications include injury to the bowel, bleeding and sepsis. Though, it was initially introduced as a diagnostic test for direct inspection of the peritoneum and biopsy procedures, advances in techniques and training of surgeons lead to the development of laparoscopic surgery involving almost all organs, both solid and hollow.

Laparoscopic surgery (key hole surgery) done by trained surgeons is safe, less traumatizing and cosmetically more acceptable. Postoperative pain is considerably less. Convalescence and hospitalisation are shorter than for conventional surgery. There is advantage in cost.

SECTION

4

Hepatobiliary System

CHAPTER

8 Hepatobiliary System: General Considerations

KR Vinaya Kumar

General considerations, Pattern of diseases affecting the liver and biliary system in India

GENERAL CONSIDERATIONS

Liver occupies the right hypochondrium and epigastrium and it weighs around 1.5 kg in adults. It is in close apposition with the diaphragm above. It is held in place by loose folds of peritoneum. The intra-abdominal pressure prevents it from dropping. Normally, the lower border of the liver is just palpable as a soft edge below the right costal margin, on inspiration. In the epigastrium it is palpable 3 to 5 cm below the costal margin. When the abdominal muscles become lax, the liver may drop down and become more palpable. Liver is the main seat of metabolic activity. Hepatocytes are endowed with several enzymes, acting specifically in different metabolic pathways. When liver cells undergo injury or necrosis, intracellular enzymes are released into circulation, e.g. aspartate transaminase (AST) and alanine transaminase (ALT), previously known as SGOT and SGPT respectively.

Hepatic Segments

Liver anatomy can be described using two different aspects: morphological and functional. The traditional morphological anatomy is based on the external appearance of the liver. Couinaud divided the liver into eight functionally independent segments. Each segment has its own vascular inflow, outflow and biliary drainage. In the center of each segment there is a branch of the portal vein, hepatic artery and bile duct. In the periphery of each segment there is vascular outflow through the hepatic veins (Fig. 8.1).

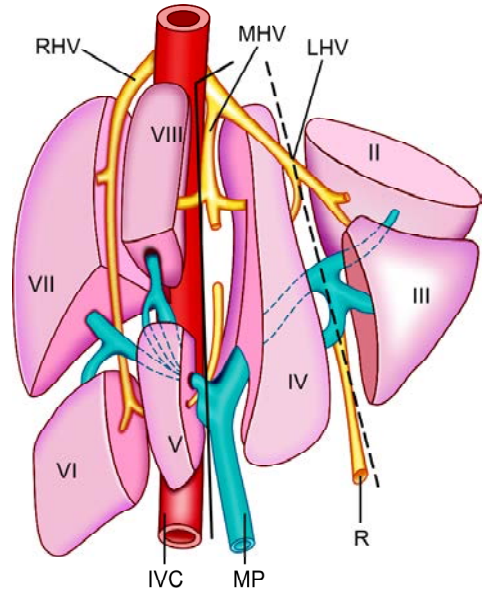


Fig. 8.1: Segmental anatomy of liver. IVC—inferior vena cava, MP—main portal vein, RHV, MHV and LHV—right, middle and left hepatic veins

Major functions of liver are discussed below.

Carbohydrate Metabolism

Glycogen formation and release of glucose from glycogen.

Protein Metabolism

Synthesis of albumin, deamination and transamination of amino acids and peptides. Production of complement and other proteins. Conversion of ammonia into urea for excretion.

Fat Metabolism

Metabolism of cholesterol and lipoproteins.

Secretion of Bile

Bilirubin which is derived from the breakdown of hemoglobin and myoglobin by the reticulo-endothelial system is conjugated by liver cells into water soluble products (conjugated bilirubin-cholebilirubin) and excreted into bile canaliculi. Ultimately, these are discharged into the second part of the duodenum for elimination.

The bile pigments secreted into the intestine are converted into urobilinogen by bacterial action. Part of it is absorbed passively in the portal circulation and reaches the liver cells. This pigment is re-excreted into bile canaliculi (entero-hepatic circulation). A part of urobilinogen escapes the hepatic cells and reaches the systemic circulation to be excreted in urine as urobilinogen. Bile pigment and its further metabolites give the normal color to feces. In their absence, the feces are pale white comparable to china clay, hence called 'clay colored' stools. The pigment present in feces is called stercobilinogen. If the drainage of bile into the intestine is obstructed, the bile pigments regurgitate across the liver cells into the circulation leading to the presence of conjugated bilirubin in blood. This is obstructive jaundice. Conjugated bilirubin appears freely in urine. Unconjugated bilirubin does not appear in urine, being insoluble in water, and firmly bound to plasma albumin.

Normal level of serum bilirubin is 0.6 to 1 mg/dL. If it rises above 2 mg/dL, it manifests as jaundice. The bile salts (taurocholates and chenodeoxy-cholates) are derived from cholesterol. These are also secreted into bile. They are reabsorbed mostly at the terminal ileum. They are concerned with the emulsification of dietary fat which helps their further digestion and absorption. Fat-soluble vitamins are also absorbed along with fat. In prolonged obstructive jaundice, malabsorption of fat and fat-soluble vitamins develops.

Coagulation Function

The liver cells secrete almost all coagulation factors and also inhibitors of coagulation such as antithrombin III, protein C and protein S. The coagulation factors II, VII, IX and X are made functionally competent by the action of vitamin K in the liver. With the development of hepatic failure, prothrombin level falls and the blood coagulation process becomes impaired. Bleeding tendencies manifest. The final picture is a combination of bleeding manifestations such as gum bleeds, purpura, ecchymosis, traumatic and post-surgical bleeding with increased tendency for venous thrombosis in the portal vein and other deep veins. Procoagulant factors like von Willebrand's factor and factor VIII are found in higher amounts in blood. This leads to venous thrombosis. Reduction of prothrombin and other Vitamin K-dependent procoagulant factors and anti-thrombotic factors such as protein C and protein S_1 all tend to promote systemic bleeding tendencies.

Detoxication Function

Liver acts upon several endogenous metabolic substances, toxic products absorbed from food, and many drugs to convert them into inactive products and eliminates them through bile.

Along with the kidney, liver is a major organ for drug metabolism and elimination. Whereas most of the drugs are converted into inactive products before excretion, some drugs are made therapeutically active by passage through the liver, e.g. chloramphenicol, cyclophosphamide.

Natural estrogens are excreted in bile. With the development of hepatic failure estrogens accumulate and signs of hyperestrogenism such as gyneco-mastia, impotence and angiomatous spiders (spider naevi) develop.

Storage Function

The liver stores vitamin A, vitamin B_{12}, folates, iron and other nutrients.

HEPATIC CIRCULATION

The hepatic blood flow is 1600 mL/minute. Liver receives its blood supply from two sources—hepatic artery and portal vein. Hepatic artery provides 25% of the total blood supply and 50% of its oxygen requirement.

The portal vein is formed by the union of splenic vein and superior mesenteric vein. The portal venous blood flow is 1000 to 1200 mL/ minute. Hepatic artery, portal vein and bile duct are seen at the porta hepatis. Radicles of all these vessels are seen in relation to the hepatic lobules.

The portal venous system is unique. It carries the venous blood from the upper and lower gastrointestinal tract, spleen and pancreas. After entering the liver, the portal vein further breaks up into branches and drains blood into the sinusoids from where the blood is collected into hepatic veins for drainage. It carries products of digestion and insulin secreted by the pancreas. During the sluggish flow of blood in the sinusoids, the liver cells act upon the absorbed nutrients and further metabolic processes take place. Kupffer cells which are reticuloendothelial cells, are phagocytes which engulf particulate matter such as bacteria, preventing them from entering the systemic circulation. Normal portal venous pressure is 5 to 12 cm of water.

Venous drainage of the liver is through the hepatic veins which join the inferior vena cava directly. In chronic venous congestion, the liver is engorged with blood, later fibrosis develops, giving rise to cardiac cirrhosis. Lymphatics drain into the lymph nodes situated in relation to porta hepatis.

Portal Hypertension

When portal vein or its further branches are obstructed, back pressure develops and this leads to portal hypertension. The pressure in the portal vein and its radicles increase and reach levels above 12 cm water. Splenomegaly develops as a result of venous congestion and reticuloen-dothelial hyperplasia. There are areas where the radicles of the portal vein and systemic veins are in close apposition. In these areas, collateral vessels develop, which connect the two systems and drain portal blood into systemic veins. These manifest as varices.

The common sites for portal systemic communication are:

1. Lower 1/3 of the esophagus—esophageal varices
2. Lower end of the rectum—hemorrhoids
3. Periumbilical region—caput medusae
4. Over the bare area of the liver
5. Retroperitoneal regions.

Esophageal varices rupture and produce hematemesis and melena. Hemorrhoids bleed leading to considerable blood loss. Shunting of portal venous blood into systemic circulation without passing through the hepatic filter leads to the development of portal systemic encephalo-pathy (hepatic precoma and coma). Portal hypertension also accounts for the preferential development of ascites in the presence of hypoal-buminemia in patients with chronic liver disease.

Table 8.1: Causes of portal hypertension

• Prehepatic causes—obstruction to portal vein developing as a result of portal vein thrombosis or cavernomatous change
• Intrahepatic causes—mainly cirrhosis
• Posthepatic causes—obstruction to hepatic veins caused by thrombosis or other causes of obstruction (Budd-Chiari syndrome).

Causes of portal hypertension may be classified according to the level of obstruction (Table 8.1).

Biliary Drainage System

Bile formed by the hepatic parenchymal cells is drained into bile canaliculi which form the common hepatic duct which emerges from the porta hepatis. The cystic duct from the gallbladder joins it to form the common bile duct which passes down to open in the second part of the duodenum along with the pancreatic duct, at the ampulla of Vater. This opening is controlled by the sphincter of Oddi. Bile secretion goes on continuously, but drainage into the duodenum coincides with the entry of food. Bile collects in the gallbladder during the intervals and gets concentrated. Gallbladder and the common bile duct are common sites for formation of biliary calculi. Normally the gallbladder is not palpable. When it enlarges as a result of obstruction, its fundus becomes palpable below the lower margin of the liver, just outside the right border of rectus abdominis muscle. Sometimes in chronic obstruction, the gallbladder may enlarge to large size and may reach even as low as the right iliac fossa. It can be seen moving under the abdominal wall and palpated as a tense cystic rounded mass, quite distinct from the lower edge of the liver. Inflammation of the gallbladder, (i.e.cholecystitis) may have an acute or a chronic presentation. It is often associated with gallstones. Gallstones in the common bile duct cause biliary colic, cholangitis and obstructive jaundice. In India and other tropical countries, presence of round worms (*Ascaris lumbricoides*) in the common bile duct many give rise to biliary colic rarely, especially in children.

PATTERN OF DISEASES AFFECTING THE LIVER AND BILIARY SYSTEM IN INDIA

A special type of cirrhosis termed Indian childhood cirrhosis seen in childhood used to be common in

some parts of South India. Its incidence has come down. Several toxins such as aflatoxins present in food cause acute and chronic hepatic damage. Veno-occlusive disease occurs in small outbreaks. Noncirrhotic portal fibrosis (NCPF) is also more common in India.

Acute Liver Disease

The most common is viral hepatitis. Hepatitis A and hepatitis E which are mainly transmitted by the feco-oral route are common, affecting children and young adults. Epidemics may occur when the drinking water is contaminated with sewage.

Hepatitis B virus (HBV) is also common. The prevalence of HBsAg positivity ranges in the general population from 4 to 6% as is shown in small isolated studies. Vertical transmission from mother to infant is common. Other modes of transmission include the use of contaminated needles, transfusion of blood and blood products and also through the sexual route. The coexistence of HIV and HBV is common. This has brought in additional problems in the management of such patients.

Hepatitis C also is increasingly recognized. Outbreaks of hepatitis C have been reported. Many cases of transfusion induced hepatitis are due to hepatitis C.

Acute hepatic failure as a result of viral hepatitis, poisoning, and *Plasmodium falciparum* malaria is frequently seen. Hepatic amoebiasis may occur in young and middle aged adults, more so in men. It used to be a common cause of tender hepatomegaly without jaundice. Amoebic liver abscess used to be very common before 1970. At present it is seen much less frequently. Alcoholism predisposes to it.

Tumors

Primary carcinoma is a common neoplasm in the younger age groups. Secondary carcinoma is seen more in older age groups.

Chronic Liver Disease

Among the chronic liver diseases, cirrhosis tops the list. All types of cirrhosis are seen. Viral hepatitis and alcoholism account for the majority. Portal hypertension developing in noncirrhotic portal fibrosis (NCPF) is a less common cause for massive splenomegaly and hematemesis.

Hepatic Failure

Viral hepatitis and poisoning by drugs, chemicals and toxins account for the majority of causes of acute hepatic failure. Cirrhosis liver is the most frequent cause for chronic hepatic failure.

Gallbladder and Biliary Tract

Diseases of the gallbladder and biliary tract are frequent. Gallstones may be detected in a good number of persons (10–15%) or routine ultrasound of the abdomen, but these may be silent in the vast majority. Calculous cholecystitis accounts for many cases of gallbladder dyspepsia.

CHAPTER

9

Noninvasive Investigations in Diseases of Hepatobiliary System

KR Vinaya Kumar

Biochemical tests, Coagulation factors, Viral screening, Tests for hereditary metabolic liver diseases

BIOCHEMICAL TESTS

Tests that Measure Detoxification or Excretory Function

Serum Bilirubin

Bilirubin is the breakdown product of porphyrin ring of heme containing proteins. It is found in the blood in two fractions—conjugated and unconjugated. Serum bilirubin is raised above 2 mg*l*dL in jaundice. The level of serum bilirubin gives objective evidence of the severity of jaundice and helps to assess the progress with treatment. Conjugated and unconjugated bilirubin can be estimated to find out the type of jaundice. This differentiation is more important when investigating the cause of congenital hyperbilirubinemias.

Bilirubin in Urine

Any bilirubin found in the urine is conjugated bilirubin. The presence of bilirubinuria implies the presence of liver disease. A urine dipstick test can be used for the detection of presence of bilirubin.

Blood Ammonia

The liver plays a role in the detoxification of ammonia by converting it to urea, which is excreted by the kidneys. There is only a poor correlation between serum ammonia and hepatic function.

Serum Enzymes that Reflect Damage to Hepatocytes

Aspartate aminotransferase (AST) previously known as serum glutamic oxaloacetic transaminase (SGOT), alanine aminotransferase (ALT) previously known as serum glutamic pyruvic transaminase (SGPT).

ALT is found primarily in the liver. AST is found in many other tissues such as muscles, heart and others. So ALT is comparatively more specific for liver than AST. Progressive rise in levels of these enzymes suggests continuing hepatic necrosis. In viral hepatitis, estimation of ALT levels helps to identify activity of the disease. Even in the absence of any other clinical sign, persistent raised levels of ALT should suggest continuing liver injury and this should be the indication for further investigations.

In fulminant hepatic necrosis, when most of the liver cells are necrosed, the level of ALT may even fall and therefore, in such circumstances estimation of this enzyme is not of much help in assessing the severity.

Striking elevation of aminotransferases (>1000) is seen in acute viral hepatitis, ischemic liver injury or paracetamol toxicity.

The pattern of elevation of these enzymes can be helpful diagnostically. In most acute hepatocellular disorders ALT is higher than or equal to AST. AST: ALT ratio >2:1 is suggestive while a ratio >3:1 highly suggestive of alcoholic liver disease. In chronic viral hepatitis even two times upper limit of normal ALT should be considered significant.

Serum Enzymes that Reflect Cholestasis

These include alkaline phosphatase (ALP) and 5′-nucleotidase gamma glutamyl transpeptidase

(GGT). Normal level of alkaline phosphatase (ALP) in serum is 4 to 13 King Armstrong Units (KAU) or 35 to 125 IU/L. The source of alkaline phosphatase in blood is primarily from the bone and liver. Hepatic alkaline phosphatase is increased in obstructive jaundice. Values above 30 KAU are suggestive of obstruction to biliary drainage. ALP is a more sensitive and reliable parameter to diagnose biliary obstruction than serum bilirubin level. ALP is also elevated in hepatocellular carcinoma.

5′-nucleotidase and GGT are rarely elevated in conditions other than liver disease.

Tests that Measure Biosynthetic Liver Function

- Serum albumin
- Serum globulins
- Gamma globulins (immunoglobulins)
- Alpha globulins
- Beta globulins.

Serum albumin is synthesized exclusively by hepatocytes. Albumin has a long half-life (18–20 days), with 4% degraded per day. In liver failure, albumin level usually falls below 3.5 g/dL. The serum albumin correlates well with hepatic synthetic function. Globulins are increased in cirrhosis liver. There is reversal of *A/G* ratio. Beta and gamma globulins contribute to this increase. In primary biliary cirrhosis, IgM is increased.

COAGULATION FACTORS

Serum Prothrombin Time

This is a sensitive index of acute and chronic liver diseases. In prolonged obstructive jaundice, if vitamin K absorption is defective, prothrombin time is prolonged. If prothrombin time remains prolonged even after parenteral administration of vitamin K, it indicates hepatic parenchymal damage. The severity of depression of prothrombin level correlates with the severity of hepatic failure. It is also a good index for prognosis.

VIRAL SCREENING

Hepatitis B Virus (HBV)

HBsAg-surface antigen. Detected by ELISA—indicates the occurrence of infection. Anti HBc—antibody against core antigen. Detection of anti-HBc IgM is diagnostic of HBV hepatitis.

Table 9.1: Serological markers of HBV infection

Surface antigen	HBsAg	Screening test for HBV infection—presence of recent or past infection
e antigen	HBeAg	Suggest infectivity. Presence of HBeAg is evidence of viral multiplication in the liver.
Core antigen	HBcAg	Not seen in blood
Antibody to HBsAg IgG	Anti-HBs IgG	Indicates presence of protective antibody
Antibody to HBcAg IgM	Anti-HBc-IgM	Signifies the occurrence of active infection
Antibody to HBcAg IgG	Anti HBc-IgG	In low titers suggestive of past infection, high titers suggest continuing infection
Antibody to HBeAg Anti-HBe	Anti-HBe	Loss of infectivity. Virus may be in the integrated phase

HBe antigen is indicative of active replication of the virus and infectivity. Persistence of HBe-Ag beyond ten weeks might suggest progression to carrier state or chronic hepatitis (Table 9.1).

HBV DNA (qualitative and quantitative PCR): Serum HBV DNA is an indication of HBV replication and it helps to quantitate the viral load. Determination of the viral load is important in deciding treatment options and accessing cure.

Hepatitis C Infection (HCV)

The presence of anti HCV in serum indicates exposure to the virus but does not differentiate among acute, chronic and resolved infections. Serological assays typically are used for screening and first line diagnosis, whereas virologic assays are required for confirming infection, and initiating and monitoring treatment.

Indirect Assays

Enzyme immunoassays (EIA) detect antibodies against different HCV antigens from the core and structural proteins. The latest third generation EIAs detect antibodies against HCV as early as 7 to 8 weeks with a sensitivity and specificity rates of 99%.

Direct Assays

Qualitative Assays

1. PCR amplification: Detects HCV RNA level as low as 50 IU/mL.

2. Transcription mediated amplification (TMA): This test has a detection limit if 10 IU/mL.

The specificity rate is 99% for both tests.

Quantitative Assays

Useful for monitoring antiviral therapy.

1. Signal amplification: Represented by the third generation branched chain DNA (bDNA) assay.
2. Target amplification: The lower limit of detection of HCV RNA with current assays ranges from 30 to 615 IU/mL.

HCV Core Antigen Assay

HCV core antigen can be detected and quantified with an EIA.

HCV Genotyping

Genotyping is important for determining the drug dosage and duration of antiviral therapy since the response to drugs and immunomodulators differ with different genotypes.

Hepatitis A and E Infection

Acute HAV and HEV infection can be diagnosed by testing IgM anti HAV and IgM anti HEV antibody respectively.

Detection of Specific Antibodies

Autoimmune hepatitis and primary biliary cirrhosis can be diagnosed and followed up (Table 9.2).

Hepatitis D-virus (Delta Virus) Infection (HDV)

This occurs as coinfection or super infection in HBV infected persons. It is important to detect HDV since this combination produces more serious outcome.

Table 9.2: Diagnostic markers useful in autoimmune hepatitis and primaty biliary cirrhosis

Antinuclear antibody (ANA)	Autoimmune hepatitis Type I
Anti smooth muscle (ASMA) antibody	
Liver-kidney-microsomal antibody (LKM-1)	Autoimmune hepatitis Type II
Soluble liver antigen (SLA)	Autoimmune hepatitis Type III
Antimitochondrial antibody (AMA)	Primary biliary cirrhosis

Anti-HDV IgG antibody detection and real time PCR for the virion are diagnostic. HDV can be genotyped by molecular assays.

TESTS FOR HEREDITARY METABOLIC LIVER DISEASES

Screening tests for common hereditary and metabolic disorders such as hemochromatosis, alpha-1-antitrypsin deficiency and Wilson's disease should be done in all forms of chronic liver disease. If the screening test is positive the supportive and definitive tests should also be done for confirmation. (Table 9.3).

Table 9.3: Biochemical changes in metabolic liver disease

Disease	*Screening test*	*Supportive test*	*Confirmatory test*
Primary hemochromatosis	Serum ferritin > 400 mcg/L	Iron saturation > 55%	Hepatic iron index >1.9
Alpha 1-antitrypsin deficiency	Serum electrophoresis	Phenotyping (Pi type)	Liver biopsy showing PAS positive diastase resistant inclusion bodies
Wilson's disease	Slit lamp examination of cornea for K-F ring ceruloplasmin<10 L)	24 hrs urine copper estimation >40 mcg/dL 24 hrs	Quantitative copper estimation in liver biopsy > 250 mcg in 1g of dry liver tissue

CHAPTER

10

Invasive Investigations in Diseases of Hepatobiliary System

KR Vinaya Kumar

Percutaneous transhepatic cholangiography, Liver biopsy

PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY (PTC)

PTC is done in patients with jaundice caused by obstruction of main bile ducts. But this is possible only if the intrahepatic bile ducts are seen to be dilated in USG. The site of obstruction can be localized and differentiated.Transhepatic drains can be placed to treat cholangitis and sepsis, stents can be placed and gall stones can removed. This technique now used only if ERCP has failed.

Liver Biopsy

Liver biopsy is an invasive diagnostic procedure which carries mortality about 5 to 10 times that of an elective laparotomy. Hence, it should be resorted to only if all noninvasive investigations fail to give a proper diagnosis. It is done with a biopsy gun under direct ultrasound guidance. Previously Trucut, Menghini, and Vim-Silverman needles were used.

Precautions

Platelet count and prothrombin time should be checked before biopsy. If prothrombin time is prolonged, it should be corrected with vitamin K and fresh frozen plasma. In the presence of any hemorrhagic tendency, supply of fresh blood and coagulation factors should be available at hand.

Indications

1. Chronic viral hepatitis: This is probably the commonest indication in India at present. Biopsy is required to establish the diagnosis and for histopathological evaluation of necrosis and fibrosis *(Knodell's scoring system)*. It will give indications for antiviral treatment in both chronic HBV and HCV infections. Repeated biopsies may be required to assess treatment response.
2. Abnormal liver function tests: Persistent elevation of ALT, AST and ALP require further evaluation. Often other investigations are inconclusive and biopsy may be required. Conditions such as nonalcoholic fatty liver disease, primary sclerosing cholangitis and hepatic granulomas can be confirmed only by biopsy.
3. Metabolic liver disorders: In hereditary metabolic liver diseases such as hereditary hemochromatosis (HHC) and Wilson's disease liver biopsy is done to assess the hepatic iron index and copper content respectively.

4. Family members of HHC or Wilson's disease:. In order to assess their metabolic state and prophylaxis liver biopsy is needed. At present gene screening methods are available in selected centers. These are noninvasive and therefore, are preferable.
5. Liver biopsy may be required for the diagnosis of systemic illnesses such as pyrexia of unknown origin. Obscure cases of miliary tuberculosis may reveal glanulomas in the liver.
6. For monitoring of transplanted liver and to detect rejection early.
7. In jaundice complicating pregnancy, biopsy may be required for distinguishing acute fatty liver of pregnancy (AFLP) from the various types of hepatitis.

When liver disease is advanced and there is coagulation failure percutaneous liver biopsy is unsafe. Transjugular liver biopsy can be done with a biopsy device introduced into the jugular vein.

SECTION

5

Respiratory System

CHAPTER

11 General Considerations

C Sudheendra Ghosh, KV Krishna Das

Conducting system—airways, nasal cavity and paranasal sinuses, Larynx, Trachea and bronchi, Lungs, Pleura, Physiological considerations, Air entry and production of breath sounds, Control of ventilation and respiratory rhythm, Surfactant, General pattern of respiratory diseases in India

INTRODUCTION

The thorax is an osseocartilaginous cage which extends from the root of the neck to the abdomen. It houses the principal organs of respiration—the lungs, which are separated from each other by the mediastinum. The thoracic cage is constructed in such a way that its movements result in increase and decrease of the anteroposterior and lateral diameters and its vertical height, thereby increasing or decreasing the intrathoracic volume during inspiration and expiration.

In inspiration, the anteroposterior and transverse diameters of the thorax are increased. Movements of the ribs at the costovertebral joints result in increased anteroposterior diameter (pump-handle movement). The transverse diameter is further increased by the ribs swinging outwards (bucket-handle movement). The diaphragm which is attached to the lower margin of the thoracic cage acts like a piston. The vertical diameter increases by the contraction of diaphragm which results in opening up of the costodiaphragmatic recesses, and elongation and narrowing of the mediastinum.

During quiet respiration, expiration is brought about by the elastic recoil of the chest wall and the lungs. During forced expiration abdominal muscles pull the ribs down and the relaxed diaphragm is pushed up to reduce the vertical height.

Conducting System—Airways

This extends from the nose to the terminal bronchioles. This can be divided into upper and lower respiratory tracts. The upper respiratory tract consists of the nose, paranasal sinuses, nasopharynx and larynx. The lower respiratory tract includes trachea, bronchi and bronchioles up to the terminal bronchioles. The larger air passages are provided with rigid cartilaginous rings which prevent them from collapsing during strong respiratory movements. The bronchi branch repeatedly in a dichotomous manner becoming smaller and narrower progressively.

Air passages less than 1 mm in diameter are termed bronchioles. The bronchioles and the distal passages are devoid of cartilage. One bronchiole enters each lung lobule. This lobular bronchiole leads to terminal bronchioles which further subdivide into respiratory bronchioles which open into alveolar ducts. These ducts are thin walled tubes ending in alveolar sacs which are studded with small pouches known as acini or alveoli. It is estimated that with about 350 million alveoli in the adult lungs, the surface area provided for gas exchange goes up to 100 m^2.

Nasal Cavity and Paranasal Sinuses

The nasal cavity is concerned with respiration, olfaction, exchange of heat and water vapor, and

to a small extent, modification of the voice. See Chapter 51.

The Larynx

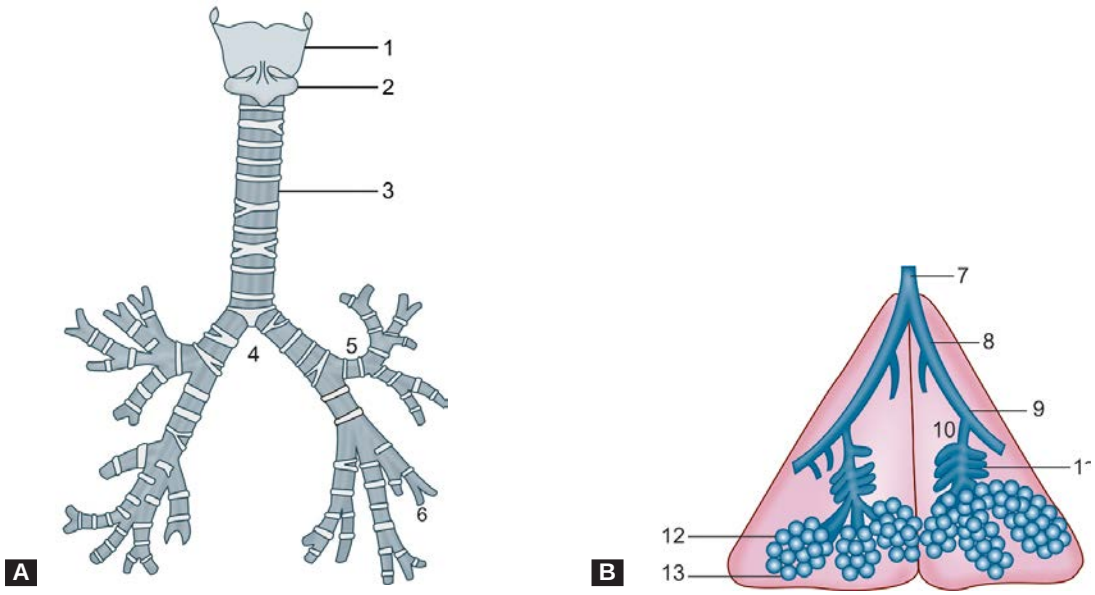
It is that part of the respiratory tract which connects the pharynx to the trachea. In the adult it is situated opposite the third to sixth cervical vertebrae. It is a cartilaginous structure, made up of thyroid, cricoid, arytenoid and epiglottic cartilages. It acts as an air-passage and it has a sphincteric mechanism. Essentially it is an organ of phonation. The vocal cords which are supported on cartilages and supplied with muscles serve to produce sounds. Tension of the cords and the vocal aperture can be altered by muscular action and this helps to alter the quality of sounds. By closing the vocal aperture, entry of foreign bodies into the trachea can be prevented. Normally, breathholding is possible by closing the vocal aperture. In bilateral vocal cord paralysis breath-holding is not possible.

Trachea and Bronchi

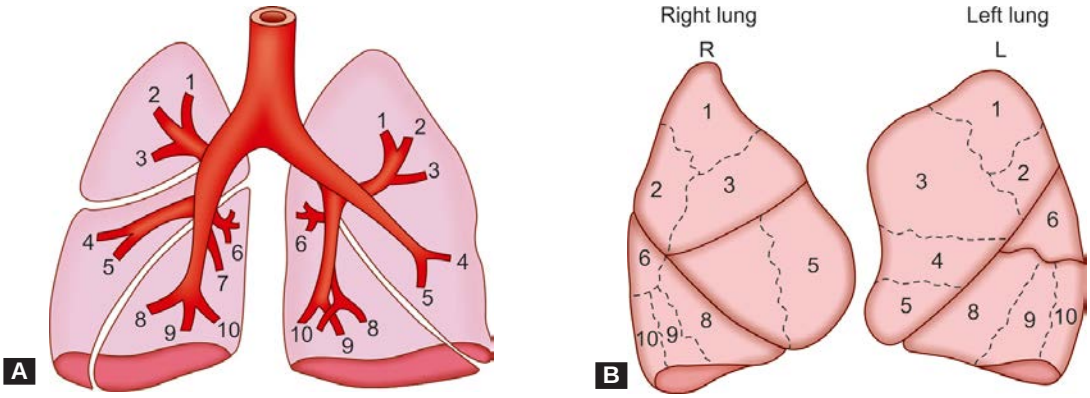
The trachea is 10 to 11 cm long and is made up of cartilaginous and membranous walls. It continues downwards from the larynx and extends from sixth cervical vertebra to the upper border of fifth thoracic vertebra, where it divides into two principal bronchi (Figs 11.1A and B). The trachea is in the median plane, though at the bifurcation it is a little to the right. It is slightly flattened posteriorly. In adults the lumen is about 12 mm. The right principal bronchus is about 2.5 cm long. It is wider and shorter than the left and it proceeds as the direct continuation of the trachea. Hence, inhaled foreign bodies enter the right bronchus more frequently than the left. The left main bronchus which is about 5 cm long, enters the hilum of the left lung opposite the sixth thoracic vertebra. It runs more horizontally than the right. The main bronchus divides into lobar bronchi and further into segmental bronchi. Each segmental bronchus supplies a self-contained, functionally independent unit of lung tissue termed the bronchopulmonary segment. Figures 11.2 and 11.3 give the anatomy of the lungs.

THE LUNGS

Each lung lies freely in the corresponding pleural cavity. The right lung weighs about 625 g and the left, 565 g. The right lung has three lobes—upper,



Figs 11.1A and B: Tracheobronchial tree. Bronchopulmonary anatomy (1) Thyroid cartilage, (2) Cricoid cartilage, (3) Trachea, (4) Right and left principal bronchi, (5) Lobar bronchus, (6) Segmental bronchus, (7) Terminal bronchus, (8) Lobular bronchiole, (9) Respiratory bronchiole, (10) Alveolar duct, (11) Atrium, (12) Alveolar sac, (13) Alveolus



Figs 11.2A and B: (A) Segmental anatomy of the lungs with divisions of the bronchi; (B) Lateral surface of the lungs showing bronchopulmonary segments

Right lung	*Left lung*
Upper lobe	Upper lobe
1. Apical	1. Apical
2. Posterior	2. Posterior
3. Anterior	3. Anterior
Middle lobe	Lingula
4. Lateral	4. Superior (of lingula)
5. Medial	5. Inferior (of lingual)
Lower lobe	Lower lobe
6. Apical	6. Apical
7. Medial basal	7. See note
8. Anterior basal	8. Anterior basal
9. Lateral basal	9. Lateral basal
10. Posterior basal	10. Posterior basal

middle and the lower. The left lung has only two lobes—the upper and the lower. The portion corresponding to the middle lobe on the right is incorporated in the left upper lobe as the lingular segments (Table 11.1 and Figs 11.2A and B)

Table 11.1: Main divisions of the right and left bronchi and the major bronchopulmonary segments

Right main bronchus and segments		*Left main bronchus and segments*	
Upper lobe	Apical Posterior Anterior	Upper lobe	Apical Posterior Anterior
Middle lobe	Medial Lateral	Lingula	Superior Inferior
Lower lobe	Apical (superior) Medial basal Anterior basal Lateral basal Posterior basal	Lower lobe	Apical (superior) Medial basal Anterior basal Lateral basal Posterior basal

Note: In about 90% of the population the anterior basal bronchus arises in common with left medial basal bronchus which supplies the left medial basal segment. In 10% the left medial basal bronchus arises separately.

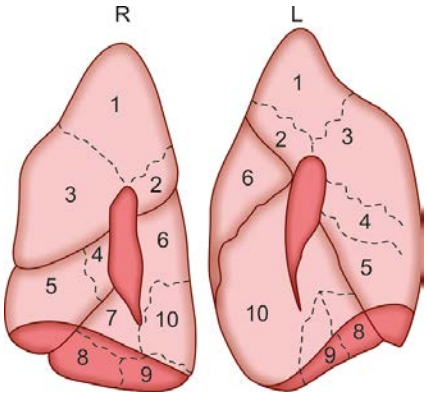


Fig. 11.3: Medial surface of the lungs showing bronchopulmonary segments

Right lung	*Left lung*
Upper lobe	Upper lobe
1. Apical	1. Apical
2. Posterior	2. Posterior
3. Anterior	3. Anterior
Middle lobe	Lingula
4. Lateral	4. Superior (of lingula)
5. Medial	5. Inferior (of lingula)
Lower lobe	Lower lobe
6. Apical	6. Apical
7. Medial basal	7. See note
8. Anterior basal	8. Anterior basal
9. Lateral basal	9. Lateral basal
10. Posterior basal	10. Posterior basal

The parts of each lung are apex, base, hilum, three borders and two surfaces. The apex is rounded. It rises above the thoracic inlet and lies 2.5 cm above the medial third of clavicle. The base which is concave and semilunar, rests on the diaphragm. Costal surface corresponds to the shape of the inner aspect of the chest wall. The medial surface has two parts, the posterior portion being in apposition with the vertebral bodies and the anterior portion with the mediastinum. At the hilum the bronchi, pulmonary vessels, lymphatics and nerves pass to and from the lung. The borders are anterior, posterior and inferior. The posterior border is rounded whereas the other two are sharp.

The right lung consists of three lobes and two fissures. The oblique fissure runs from the interval between the third and fourth thoracic vertebrae, downwards and forwards. At the mid axillary line it lies in the fifth intercostal space. It ends anteriorly behind the sixth costal cartilage. The horizontal fissure extends from the oblique fissure in the mid axillary line in the fifth intercostal space and runs to the fourth costochondral junction auteriorly.

The left lung is divided into upper and lower lobes by the oblique fissure which runs like that on the right. All the lobes are further divided into bronchopulmonary segments each of which is supplied by the corresponding segmental bronchus. Pathology confined to definite ares in the lung.

Surface Marking of Lungs

Apex of the upper lobe is marked by a dome rising 2.5 cm above the medial third of clavicle.

Anterior border: This may be represented by joining three points:

i. Point at sternoclavicular joint
ii. Point in median plane at sternal angle
iii. Point in median plane at xiphisternal joint.

Note: Anterior border of left lung presents a cardiac notch from 4th to 6th costal cartilages in front.

Lower border: It crosses sixth rib in mid-clavicular line, eighth in mid-axillary line, tenth at lateral border of erector spinae and ends 2 cm lateral to tenth thoracic spine.

Posterior border: I runs upwards from a point 2 cm lateral to the tenth thoracic spine, along the posterior margin of pleural reflection.

Abnormalities in the lungs often manifest as abnormal physical findings over the corresponding portions on the chest.

Anatomy of the Pleura

Pleura is a serous membrane lining the thoracic cavity which forms two pleural sacs, one on either side of the mediastinum and invaginated on its medial aspect by the lung. It has two layers—pulmonary or visceral and parietal pleura. The pulmonary pleura is closely adherent to the lungs. The parietal pleura lines the inner aspect of the chest wall. At the hilum both these layers are continuous. In between these two layers is a potential space known as pleural cavity which contains a small quantity of fluid. Intrapleural pressure is always negative compared to atmo-spheric pressure and this negative pressure keeps the lungs distended. This negative pressure is abolished when air enters the pleural sac, under pathological circumstances as in pneumothorax.

Surface Marking of the Parietal Pleura

Cervical Pleura

The cervical pleura rises in a dome shaped manner 2.5 cm above the medial third of the clavicle.

Anterior margin: It is obtained by joining three points:

i. Point at sternoclavicular joint
ii. Mid point of sternal angle
iii. Point at the xiphisternal junction.

Inferior margin: It passes backwards and laterally, crosses eighth rib in midclavicular line, tenth rib in midaxillary line and ascends slightly to cross the twelfth rib and ends 2 cm lateral to 12th thoracic spine.

Posterior margin: passes upwards from a point 2 cm lateral to 12th thoracic spine, to 2 cm lateral to 7th cervical spine.

Surface Marking of the Different Lobes and Segments on the Chest Wall

Front of the Chest

Supraclavicular region (medial third)	Anterior portion of the apical segment of the upper lobe
Clavicle and infraclavicular region up to the 3rd rib	Anterior portion of the upper lobe
Mammary region 3rd to 6th rib	Anterior portion of the middle lobe on the right. Lingular segments of the upper lobe on the left

Inframammary region 6th rib to costal margin	Part of middle lobe on the right, and lingular segment of the upper lobe on the left. Parts of lower lobes on both sides

Lateral Aspect

Axilla-up to 6th rib below	Lateral aspect of the upper lobe.
Infra-axillary region 6th rib to costal margin	In front, lateral aspect of the middle lobe on the right and lateral aspect of the lingular segments on the left. Behind and below these regions, the lateral aspects of the lower lobes on both sides

Posterior Aspect

Suprascapular region—portion above the upper border of scapular spine	Apical segment of upper lobe
Interscapular region—region between the medial border of scapula and vertebral spines 02-07	Posterior aspect of the apical segment of the lower lobe
Infrascapular region—portion below angle of scapula, i.e. below 07 spine	Posterior aspect of the basal segment of the lower lobes

PHYSIOLOGICAL CONSIDERATIONS

Ventilation is the mass movement of air in and out of the air passages. It depends upon the:

- Effectiveness of the respiratory movements
- The bony structures of the thoracic age
- The physical state of the lungs
- The respiratory muscles-diaphragm and the muscles of the chest wall
- Patency of the air passages
- Integrity of the neurological connections which innervate the muscles of respiration
- Functioning of the respiratory centers situated in the brain.

All contribute to the effectivness of ventilation. In the normal adult 6 to 10 liters of air is moved in and out in one minute.

Perfusion of Blood in the Pulmonary Capillaries

A volume of blood equal to the cardiac output perfuses the pulmonary arterioles and capillaries. The blood is separated from air in the alveoli by a thin layer composed of the vascular endothelium and alveolar lining cells with intervening basement membrane and pulmonary interstitium (the alveolocapillary membrane). Diffusion of gases across this membrane occurs rapidly within a fraction of the time the blood takes to travel through the capillary bed. Diffusion of oxygen, carbon-dioxide and other volatile substances across the alveolocapillary membrane is also instantaneous in normal subjects. Conditions which lead to impairment of diffusion include pulmonary edema, interstitial fibrosis, hyaline membrane disease, acute respiratory distress syndrome (ARDS), progressive pulmonary vascular occlusions and several others.

Ventilation, perfusion with blood and diffusion of gasses should all be optimal in order to ensure adequate respiratory function.

Air Entry and Production of Breath Sounds

About 500 mL of air passes into the respiratory tract during each inspiration. Only about 350 mL reaches the alveoli. The rest remains in the trachea and bronchi which forms the dead space, since gas exchange does not take place in the larger airways.

Breath Sounds

These are produced by the movement of air in the larger air passages. Turbulence of air and the consequent vibration of the vocal cords and various tissues are responsible for the production of sounds. Two types of breath sounds can be heard over the chest on auscultation—vesicular and bronchial. Vesicular breath sound is heard over areas of normal lung tissue which attenuates and filters part of the sounds. On the other hand, bronchial breath sounds (also known as laryngeal) are heard over the chest when the normal processes of attenuation and filtration do not take place. In pathological states such as consolidation, collapse and fibrosis of the lungs, the processes of attenuation do not take place as in normal lung.

Control of Ventilation and Respiratory Rhythm

Two major groups of cells connected with respiratory control are situated in the medulla oblongata. The dorsal respiratory group contains predominantly inspiratory cells while the ventral respiratory group contains both inspiratory and expiratory groups of cells. The rhythmicity of respiration depends upon inhibitory and excitatory interactions between these respiratory cells. From the respiratory center, impulses reach the spinal motor neurones via the reticulospinal tracts. Besides

these, there is a pneumotaxic center in the pons, the exact function of which is not fully understood.

Many factors influence their activity. Among them are neural inputs from higher centers, chemoreceptors and vagal influences which are described below.

Higher Centers

Most areas are inhibitory to respiration though some motor and premotor areas may be excitatory.

Chemoreceptors

i. Carotid chemoreceptors are present in carotid bodies which are situated at the bifurcation of common carotid artery. Ventilation is stimulated when these receptors are excited by hypoxia, hypercapnia or acidosis. The principal stimulus for respiration in health is fall in arterial oxygen saturation (PaOJ).
ii. Central chemoreceptors are present on the ventral surface of medulla. They are influenced by changes in arterial carbon dioxide ($PaCO_2$) and H^+ ion concentration in both arterial blood and cerebrospinal fluid. Presence of CO_2 in inspired air is a very strong stimulus to increase ventilation.

Vagus and Sympathetic Nerves

These give rise to filaments which ramify to form pulmonary plexuses and accompany the ramifications of the bronchi. Vagus supplies motor fibers to broncho-constrictor muscles. Afferents to the bronchial mucosa and alveoli are derived from these plexuses.

i. *Pulmonary stretch* receptors are located in the bronchi. Bronchopulmonary inflation and deflation reflexes (Hering-Breuer) are prominent in infants and anesthetized persons but they are less pronounced in normal adults.
ii. *J-receptors* are responsible for rapid shallow breathing and these are stimulated by pulmonary congestion, edema or microemboli.
iii. There are some receptors which are activated by irritants in inhaled air.
iv. There are also receptors which initiate cough reflex.

Surfactant

This is composed of phospholipids synthesized by type II pneumonocytes. Surfactant lowers surface tension and thereby enables the alveoli to remain fully patent without collapsing. Synthesis of surfactant begins only after 16 weeks of gestation and it is released from the alveolar wall only after the 26th week. Therefore, babies born before 26th week of gestation are at risk of *acute respiratory distress syndrome.*

GENERAL PATTERN OF RESPIRATORY DISEASES SEEN IN INDIA

During childhood, respiratory infections are common and they account for considerable morbidity and mortality. In undernourished children, acute respiratory infections carry higher mortality.

Tonsillitis, bronchitis, bronchopneumonia and lobar pneumonia account for the majority of respiratory illnesses during childhood. Primary tuberculosis affects children more frequently than adults. Acute respiratory failure occurring in children may be due to respiratory distress syndrome (RDS) complicating several severe systemic illnesses, or other extensive pulmonary diseases such as broncho-pneumonia or asthma. In the syndrome of septic shock, multiorgan failure is common. Respiratory distress syndrome may develop in many of them.

In all age groups, pneumonias, bronchitis, asthma and tuberculosis are common. In adults, chronic bronchitis and emphysema, asthma, pulmonary tuberculosis, bronchiectasis and occupational lung diseases account for the major proportion of respiratory illnesses. Malignancy of lungs increases with advancing age. Acute respiratory failure in adults may be caused by asthma, bilateral pleural effusion, pneumothorax, aspiration pneumonia or acute respiratory distress syndrome (ARDS). Chronic respiratory failure in adults is mostly due to chronic bronchitis and emphysema, asthma or pulmonary fibrosis.

Pleural diseases include pleural effusion, pneumothorax, pleural fibrosis or thickening and malignancies.

With the advent of newer therapeutic interventions such as intensive care room and assisted ventilation continued for several days, special problems arise which impair cardiorespiratory function. Extensive burns as occurring in fire accidents and inhalation of noxious gases lead to damage to air passages and alveolocapillary apparatus.

CHAPTER

12 Examination of the Respiratory System

C Sudheendra Ghosh, KV Krishna Das

Cough, Expectoration of sputum, Hemoptysis, Chest pain, Dyspnea, Abnormal patterns of respiration, Sleep apnea syndrome, Wheeze, Stridor, Hoarseness of voice, Past history, Physical examination, Respiratory system examination, Inspection, Palpation, Percussion, Auscultation, A scheme for recording physical findings, Interpretation of physical findings, Common pathological changes in the lungs and pleura

RESPIRATORY SYSTEM

History: Main symptoms pertaining to the respiratory system are cough, expectoration of sputum, hemoptysis, dyspnea, pain in the chest, and wheezing.

Cough

Cough is a protective reflex mechanism. It may be induced reflexly or consciously, to dispose of foreign material or accumulated secretions in the airways. In normal persons, the secretions in the large airways are small in amount and they are cleared by mucociliary action of the bronchial mucosa. Cough arises as a result of irritation of the larger air passages or by the presence of excessive secretions in them. Cough may be of different types.

Pharyngeal Cough

The patient may present with short and dry irritative cough accompanied by pain behind the jaw or in the neck. There may be a history of nasal discharge, increase in postnasal discharge, and soreness in the throat. Pharyngeal cough is characteristic of pharyngitis and upper respiratory tract infections.

Laryngeal Cough

Laryngeal cough occurs in acute and chronic laryngitis. The cough is harsh, irritative and repetitive. It may be accompanied by stridor and cyanosis. Usually there is a history of preceding attack of pharyngitis followed by hoarseness of voice or aphonia. In whooping cough, as a result of laryngeal spasm, there is a peculiar long inspiratory whoop after a prolonged bout of severe coughing. When the cough loses its explosive nature, it is known as "bovine cough" (since it resembles cough in cattle). Bovine cough occurs in vocal cord paralysis since the laryngeal aperture cannot be closed.

Tracheal Cough

The cough may be dry and accompanied by retrosternal discomfort which increases on inspiration or coughing. Retrosternal pain and cough might increase on exposure to cold atmosphere. There may be a history of mild pyrexia and mucopurulent sputum which may be blood tinged. Presence of dyspnea and wheezing are indicative of associated bronchitis. Cough that is of metallic and hard quality is termed as "brassy cough". This is typical of tracheal obstruction, especially caused by intrathoracic tumors.

Bronchial Cough

Acute bronchitis: Cough is initially dry and nonproductive without chest pain. Later mucopurulent expectoration starts. Breathlessness and cyanosis are generally absent. Mild wheezing may be present.

Chronic bronchitis: This occurs in persons who are longstanding smokers or those working in heavily polluted atmosphere. Previous attacks of cough with

expectoration of mucoid or mucopurulent sputum recurring with every cold season is very suggestive. Cough is worse in the mornings, especially after smoking a cigarette or beedi. Sleep may be disturbed at night by persistent and paroxysmal cough. After each attack of upper respiratory infection, the sputum increases in quantity and becomes purulent, its colour changes to yellow or green. Breathlessness and wheezing may also be aggravated. Fog, smoke, and cold damp weather worsen the attacks. In between the attacks, the patient may be symptom-free and the sputum is mucoid or gray.

Pneumonia

The patient presents with high fever, chest pain, dyspnea and cough, often following an episode of upper respiratory infection. Initially the cough is dry and hacking, but later it becomes productive. Sputum is rusty brown in many cases, otherwise it may be only purulent. Frank hemoptysis may occur at times. Typical catching pain during breathing and coughing may develop during the course of the illness, this is due to development of pleurisy.

Bronchial Asthma

The patient presents with intermittent wheezing and breathlessness accompained by cough, usually worsened at night. These attacks may be precipitated by respiratory infection, exposure to cold air, smoke, dust, drugs and exercise. Sputum is sticky and mucoid. Expectoration of sputum relieves the cough and wheeze. Many close relatives may have atopic disorders.

Postural Cough

Cough brought on by adopting particular attitudes is called postural cough. If the patient presents with cough and copious expectoration which comes on by changing posture it is suggestive of bronchiectasis, lung abscess and rarely bronchopleural fistula. There may be previous history of whooping cough in childhood or aspiration of foreign material into the lungs. Common situations in which aspiration of foreign materials into the respiratory tract occurs are epileptic seizures, near drowning, vomiting following anesthesia, heavy alcoholic bouts, and lower cranial nerve paralysis. Not infrequently aspiration pneumonia may lead to lung abscess or bronchiectasis.

Bronchogenic Carcinoma

This is more common as age advances and is much more common in males. The patient presents with persistent and progressive cough associated with anorexia and weight loss. When vocal cord paralysis sets in, bovine cough develops. Sputum may be scanty in the initial stages, later it becomes blood stained, and moderate-to-massive hemoptysis may develop.

Aspiration of Foreign Bodies into the Respiratory Tract

Sudden onset of uncontrollable paroxysmal cough in an otherwise healthy person should suggest the possibility of aspirated foreign body. History of accidental inhalation of foreign body during work, play or surgical procedures in the mouth or upper respiratory tract may be present. Automobile accidents, epileptic seizures, anaesthesia and alcoholic bouts are associated with the risk of aspiration. In coma the cough reflex is abolished. If the aspiration is massive with total obstruction to the trachea or both bronchi, sudden death supervenes within minutes (Cafe coronary). Severely ill patients with confusion or coma, and lower cranial nerve palsy, may aspirate food, fluid or gastric contents if care is not taken to avoid aspiration.

If the obstruction is subtotal or partial, breathlessness, stridor, wheezing and cyanosis may develop. Sometimes patients may complain of clicking sound during breathing caused by movement of the foreign body. Obstruction to the bronchi lead to pulmonary collapse and pneumonitis. Distal to the obstruction, lung abscess or bronchiectasis may develop.

Pleural Diseases

Pleurisy and pleural effusion may be associated with cough and chest pain. Dry cough accompanied by catching pain in the axilla or under the breasts is suggestive of pleurisy.

Cardiac Failure

The patient presents with dyspnoea and cough which aggravate on exertion. The grade of dyspnoea depends upon the severity of heart failure. The expectoration is frothy, watery and blood stained. Paroxysmal nocturnal dyspnea (also referred to as

cardiac asthma) is a feature of left sided heart failure. It occurs most often within an hour or two of going to bed. By contrast, dyspnea and cough due to bronchial asthma are generally aggravated in the early hours of morning.

Otogenic Cough

This is a form of reflex cough caused by stimulation of the Arnold's nerve which is a branch of the vagus. Arnold's nerve arises from the jugular ganglion and supplies the posterior and inferior wall of the external auditory meatus. Lesions such as impacted wax in the meatus or presence of foreign bodies may evoke reflex cough, which subsides with the removal of the cause.

Habit Cough Syndrome

This is seen in patients who present with sustained repetitive coughing without any cough during sleep. This has a psychosomatic background. Most of the patients are in the age group of 6 to 17 years. Usual investigations for respiratory diseases are normal. As a result of the debilitating cough the child adopts a sick role and becomes the main focus for anxiety for the patients. Cough may be a manifestation of also a tic disorder.

Table 12.1 gives the salient clinical features of cough commonly observed in practice.

Expectoration of Sputum

Sputum is a mixture of bronchial secretions, cells and organisms which are discharged from the airways. Normal sputum may be colorless and mucoid, it is loose and nonsticky in character. Most persons do not spit out sputum. The secretions pass up from the respiratory tract by ciliary action and cough, and are swallowed. Normal quantity does not exceed a few milliliters in 24 hours.

Table 12.1: Causes of cough

Cause	*Suggestive findings*
Acute	
Upper respiratory infection (including acute bronchitis)	Rhinorrhea, red swollen nasal mucosa, sore throat, malaise
Pneumonia (viral, bacterial, aspiration, rarely fungal)	Fever, productive cough dyspnea, pleuritic chest pain, bronchial breath sounds or egophony
COPD (chronic obstructive pulmonary disease) exacerbation	Known diagnosis of COPD, diminished breath sounds, wheezing, dyspnea Pursed lip breathing. Use of accessory muscles. Tripod positioning of the arms against the legs or examination table
Foreign body	Sudden onset in a toddler who has no URI or constitutional symptoms
Pulmonary embolism	Pleuritic chest pain, dyspnea, tachycardia
Heart failure	Dyspnea, fine crackles on auscultation, extrasystolic heart sound, dependent peripheral edema
Chronic Pulmonary TB	Symptoms of weight loss, fever, hemoptysis, night sweats, exposure history, immunocompromise
Chronic bronchitis (in smokers)	Productive cough on most days of the month or for 3 months of the year/yr for 2 successive years in a patient with known smoking history. Frequent clearing of the throat, dyspnea
Postnasal drip (allergic most likely)	Headache, sore throat, cobblestoning of posterior oropharynx, pale, boggy, swollen nasal mucosa
Gastroesophageal reflux disease (GERD)	Burning chest or abdominal pain that tends to worsen with consumption of certain foods, activities, or position Sour taste, particularly on awakening, hoarseness, chronic nocturnal or early morning cough
Asthma (cough variant)	Cough in response to various provoking factors (e.g. allergens, cold, exercise) possibly wheezing and dyspnea
Hyperresponsive airways after resolution of respiratory tract infection	Dry, nonproductive cough that may persist for weeks or months after an acute respiratory tract infection
Tumors	Atypical symptoms (e.g. weight loss, fever, hemoptysis, night sweats), lymphadenopathy
Drugs, e.g. ACE inhibitors	Dry, persistent cough that may occur within days or months after initiation of ACE inhibitor therapy
Pertussis	Repeated bouts of ≥ 5 rapidly consecutive forceful coughs during a single expiration, followed by a hurried and deep inspiration ("whoop") or post-tussive emesis
Aspiration	Wet-sounding cough after eating or drinking

The various abnormalities of sputum and their significance are described below:

Mucoid Sputum

It is clear and viscous. In smokers it may be gray or black in color. Mucoid sputum is usually present in chronic bronchitis without heavy secondary infection. It is more copious in the mornings.

Watery Sputum

This is frothy, voluminous and often blood-tinged as seen in acute pulmonary edema. Rarely, frothy saliva-like sputum may be present in bronchiolo-alveolar cell carcinoma. When a hydatid cyst ruptures into a bronchus, large amounts of clear salty fluid may be expectorated. This is often accompanied by urticaria, pruritus, hypotension and signs of anaphylactic shock.

Sticky and Tenacious Sputum

Whenever infection complicates chronic bronchitis or there is exacerbation of chronic bronchial asthma, the sputum becomes sticky and tenacious. It is difficult to expectorate. Obstruction of the airways by thick secretions worsens the dyspnea. Expectoration gives relief. With clearance of infection the sputum becomes less tenacious and easier to expectorate.

Purulent Sputum

The sputum resembles pus and it is yellow or greenish. Often it is large in amount and brought out easily with cough. Purulent sputum is a sign of infection. It is seen in bronchitis, pneumonia, bronchiectasis, lung abscess, asthma with infection, bronchopleural fistula and others.

Rusty Sputum

This is suggestive of pneumococcal pneumonia. Rust color is due to admixture of altered blood with sputum. Sputum resembling red jelly (red currant jelly) results from admixture of mucus and blood and this is sometimes seen in bronchogenic carcinoma.

Foul Smelling Sputum

Severe foul smell may be present when infection is caused by anaerobic bacteria as may be seen in bronchiectasis, lung abscess or necrotizing pneumonia.

Reddish Brown Sputum

Sputum resembling reddish brown or chocolate pus (often referred to as anchovy sauce pus) is expectorated when an amoebic abscess in the liver or lung erodes into a bronchus.

Hemoptysis (Table 12.2)

Presence of blood in the sputum is termed hemoptysis. Common causes of hemoptysis are pulmonary tuberculosis, pneumonia, bronchiectasis, lung abscess, mitral stenosis and bronchogenic carcinoma. Rarer causes include inhaled foreign bodies, arteriovenous malformations, pulmonary infarction, Loefflers' syndrome, tropical eosinophilia, bronchial adenoma, aspergilloma, bleeding disorders, and ulceration of the larynx or trachea. The term *spurious hemoptysis* denotes the presence of blood caused by bleeding from the upper respiratory tract. Injuries to the lung occurring in accidents and following rib fractures give rise to hemoptysis. Hemoptysis may manifest in several forms depending on the underlying disease:

a. *Acute inflammations* like pneumonia may lead to blood mixed with sputum.
b. *Bronchiectasis and lung abscess:* In bronchiectasis the history extends over several years with the expectoration of large quantities of purulent sputum often with postural cough. Hemoptysis may be streaky or massive and blood may be mixed with sputum or may be expectorated as such. Often the general condition of the patient is satisfactory.

 In lung abscess, there is deterioration of general condition of the patient. Hemoptysis may be moderate or massive and postural cough may occur.
c. *Pulmonary tuberculosis:* In pulmonary tuberculosis, hempotysis is a common complication and the character of hemoptysis may vary. Blood may be present only in streaks or there may be massive hemoptysis. Lesser degree of hemoptysis may occur in early stages of pulmonary tuberculosis. Massive hemoptysis occurs in cavitary pulmonary tuberculosis due to rupture of blood vessels traversing the cavity (Rasmussen's aneurysms). In post-tuberculosis bronchiectasis, hemoptysis may recur even after the tuberculosis is cured with treatment.

Table 12.2: Causes of hemoptysis

Cause	*Suggestive features*
Tracheobronchial source	
Tumors	Bronchogenic carcinoma, bronchial adenoma, Kaposi's sarcoma in HIV
Bronchitis (acute or chronic)	Acute: Productive or nonproductive cough Chronic: Cough on most days of the month or for 3 months of the year for 2 successive years in patients with exposure to cigarette smoking.
Bronchiectasis	Chronic cough and mucus production in patients with a history of recurrent infections
Broncholithiasis	Calcified lymph nodes in patients with history of prior granulomatous disease
Foreign body (chronic undiagnosed, not acute)	Chronic cough (typically in an infant or young child) without URI symptoms, sometimes fever
Pulmonary parenchymal source	
Pneumonia	Presents with fever, productive cough, dyspnea and pleuritic chest pain, decreased breath sounds, bronchial breath sounds or egophony on examination
Pulmonary tuberculosis (rarely other active granulomatous disease due to fungal, parasitic, syphilitic infection) or mycetoma (fungus ball)	Associated symptoms include fever, cough, hemoptysis, night sweats, and weight loss, often history of immunosuppression
Lung abscess	Fever, cough, hemoptysis, night sweats, anorexia and weight loss, often history of aspiration, finding of consolidation followed by cavity with fluid
Goodpasture's syndrome	Fatigue, weight loss, dyspnea, on examination pallor and pulmonary crackles, anti-GBM antibody disease, hematuria and edema
Wegener's granulomatosis	Chronic sinusitis with bloody nasal discharge otitis media and nasal ulcerations, joint pains and skin manifestations (nodules, purpura), gingival thickening and mulberry gingivitis, saddle nose and nasal septum perforation, renal insufficiency following necrotizing glomerulonephritis, antineutrophil cytoplasmic antibody (ANCA) positive
Lupus pneumonitis	Fever, cough, dyspnea, and pleuritic chest pain
Primary vascular source	
Arteriovenous malformation	Presence of mucocutaneous telangiectasia or peripheral cyanosis
Pulmonary embolism	Abrupt onset of sharp chest pain, increased respiratory rate and heart rate, particularly in patients with known risk factors for pulmonary embolism.
Elevated pulmonary venous pressure (mitral stenosis, left-sided heart failure)	Crackles, signs of central or peripheral volume overload (e.g. elevated neck veins, peripheral edema), dyspnea while lying flat (orthopnea) or appearing 1–2 h after falling asleep (paroxysmal nocturnal dyspnea)
Aortic aneurysm with leakage into the pulmonary parenchyma	Back pain
Pulmonary artery rupture	Recent placement or manipulation of a pulmonary artery catheter
Miscellaneous	
Pulmonary endometriosis (catamenial hemoptysis)	Recurrent hemoptysis during menstruation
Systemic coagulopathy or use of anticoagulants or thrombolytics	Patients undergoing systemic anticoagulation for treatment of pulmonary embolism, DVT, or atrial fibrillation, patients receiving thrombolytics for treatment of stroke or myocardial infarction (MI), sometimes a family history
Leukemia and lymphoma	Symptoms of weight loss, fever and bleeding diathesis lymphadenopathy and hepatosplenomegaly

d. *Bronchogenic carcinoma:* In bronchogenic carcinoma, which is much more common in heavy smokers, hemoptysis is a common complication. There may be merely blood streaking of sputum extending for many days, or sometimes massive hemoptysis. Red jelly-like sputum may occur at times.

e. *Bronchial adenoma:* This gives rise to moderate or massive hemoptysis. When there is a history of such hemoptysis in a patient less than forty years of age, or in a female who is a nonsmoker, diagnosis of bronchial adenoma should be strongly considered. Sometimes the bleeding may be so massive that emergency

surgical measures may have to be adopted to save life.

f. *Pulmonary embolism:* This is a common complication of several diseases in which thrombosis occurs in peripheral veins with subsequent ernbolization. It may be massive and fatal, or smaller and recurrent. The latter type results in pulmonary infarction which is characterized by catching pain in the chest and streaky or large hemoptysis.

g. *Trauma to chest:* Injuries to the chest may lead to contusion of lungs. Penetrating wounds of the lungs may be caused by broken ribs or foreign particles. All these may result in hemoptysis.

h. *Left heart failure:* The sputum is frothy, watery and blood stained. Hemoptysis is due to acute pulmonary edema.

i. *Hemorrhagic diathesis:* Purpuric disorders often produce hemoptysis. Less commonly coagulation defects may also cause hemoptysis. Hemoptysis is only part of several other bleeding episodes. Positive family history and onset from early age suggest the diagnosis in hereditary hemorrhagic diseases.

j. Inhalation of irritant gases such as chlorine or sulphur dioxide leads to pulmonary edema and hemoptysis.

k. Parasite infections of the lungs give rise to milder forms of hemoptysis. This may be seen in Loeffler's syndrome (stage of larval migration of nematodes), hydatid disease, and paragonimiasis (infestation by *Paragonimus westermani*). In tropical eosinophilia mild hemoptysis may occur less commonly.

l. *Wegener's granulomatosis and Goodpasture's syndrome* may cause hemoptysis. These are rare. They belong to the group of vasculitides which are occasionally seen. Several organs are affected.

m. Hemoptysis may be induced by traumatizing the throat or upper air passages by hysterical subjects and malingerers. Vicarious menstruation is hemoptysis occurring in women during menstrual periods without any obvious pulmonary disease.

Hemoptysis is an alarming symptom which requires emergency management. Loss of more than 250 mL of blood may cause systemic effects. Massive hemoptysis occurs in cavitary pulmonary tuberculosis, bronchial adenoma, bronchogenic carcinoma, pulmonary embolism, bronchiectasis and rupture of an aneurysm into a bronchus. Careful interrogation and proper physical examination help to arrive at the diagnosis in most cases. Massive hemoptysis is an indication for urgent hospitalization and treatment.

Chest Pain (Table 12.3)

a. *Chest pain:* It arising from lung parenchyma may not be typically localized, as the lung parenchyma and the visceral pleura covering it are less sensitive to painful sitmuli. Even when there is massive destruction of lung parenchyma pain may be absent or may be only mild. Pain is more prominent and characteristic when the parietal pleura, major airways, chest wall, diaphragm or mediastinal structures are affected.

b. *Pleural pain:* It may be localized to one side or the other and is usually severe and stabbing or tearing in character, often felt in the axillae or beneath the breasts. Typically it increases with deep respiration and coughing. Movements of the thorax or trunk, like bending, stooping or turning in bed may bring on the pain. The patient tries to restrict the movements of the chest. Pleural pain may be seen in primary diseases of the pleura such as pleurisy, pleural effusion, pneumothorax and pleural tumors, or in pleural involvement secondary to pulmonary diseases such as pneumonias, pulmonary infarction and bronchogenic carcinoma. In diaphragmatic pleurisy, pain may be referred to the abdomen. A patient with pleurisy prefers to lie on the normal side, whereas when effusion develops he prefers to lie on the affected side.

c. *Root pain:* Pain in the chest may arise from irritation of the spinal nerve roots by compressing lesions. In Herpes zoster, spontaneous lancinating or shooting pain with electric shock-like sensation may occur along the nerve root distribution. Preherpetic neuralgia precedes the eruptions. Pain may start during the florid phase or may manifest as postherpetic neuralgia. The preherpetic form may be even mistaken for acute myocardial infarction.

Table 12.3: Causes of chest pain

Cause	*Presentation*	*Features*
Potentially life-threatening causes		
Acute myocardial infarction	Blood supply to the cardiac muscle is reduced or stopped mainly due to coronary occlusion	There is ischemic damage, progressive metabolic changes and death of the cardiac muscle
Angina	There is blockage or narrowing of the coronary vessels leading to imbalance between the oxygen demand of the heart and the amount of oxygen delivered via the blood	"Stable" angina occurs repetitively and predictably while exercising and goes away with rest "Unstable" angina results in unusual and unpredictable pain not relieved totally by rest or pain that actually occurs at rest
Aortic dissection	Dissection means a tear in the inner lining of the aorta. Retrosternal pain with radiation along the major arteries of neck, abdomen and down to the lower limbs	This can cause massive internal bleeding and interruption of blood flow the vital organs
Pulmonary embolism	Blood clot in one of the major blood vessels that supplies the lungs. Present with acute chest pain, breathless ness and hemoptysis	In a patient with known risk factors like cancer, immobilization, DVT, pregnancy, use of oral contraceptives or other estrogen containing drugs, recent surgery or hospitalization
Spontaneous pneumothorax	Abrupt onset of sharp chest pain, tachypnea, and tachycardia, air enters the pleural cavity and the lung is unable to re-expand	This can cut off the normal oxygen supply in the body. Cardiac tamponade if the air is under tension
Perforated abdominal viscus	Perforation of a viscus may be due to ulceration, injury or tears in any part of the gastrointestinal tract	This allows air and infected material to enter the peritoneal cavity which irritates the diaphragm, and causes chest pain
Cocaine-induced chest pain	Cocaine causes the blood vessels in the body to constrict	Decrease in coronary flow causes the pain
Causes of chest pain that are not immediately life-threatening		
Acute pericarditis	This is an acute inflammation of the percardium	Associated with fever and other cardiac symptoms
Mitral valve prolapse	Mitral valve prolapse is an abnormality in which one of the "leaves" of the mitral valve bulge's into the left atrium during contraction	Dull aching pain, mid-systolic click and mid/late systolic murmur
Pneumonias	Pneumonia is an inflammation of the lung tissue. But chest pain occurs because of inflammation of the parietal pleura	Stabbing or tearing in character. Increases with deep inspiration and coughing
Bronchogenic carcinoma	Chest pain develops when there is infiltration of neighboring structures by the tumor	Important risk factor is chronic exposure to smoke
Acid reflux disease (gastroesophageal reflux disease, GERD, heartburn)	Occurs when acidic digestive juices flow backward from the stomach into the esophagus	The resulting heartburn is localized to the epigastrium and retrosternal area
Esophagitis	Inflammation of the esophagus	
Esophageal spasm	Defined as excessive, intensified, or uncoordinated contractions of the smooth muscle of the esophagus	In both cases there is retrosternal pain or burning sensation that is aggravated on bending forward or lying in supine position
Costochondritis	There is inflammation of the cartilage between the ribs and sternum. Pain is typically located in the mid-chest, with intermittent waxing and waning	Pain may be increased with deep breaths, movement, and pressure
Herpes zoster	Also known as shingles, due to infection of the dorsal root ganglion of the sensory roots by chicken pox virus. The pain is spontaneous lancinating, severe, felt in the affected dermatome Preherpetic neuralgia may precede the rash by 4–7 days.	Risk factors include immunocomprised states such as advanced age, HIV, or cancer
Conditions like acute chest syndrome in sickle cell anemia	Due to blocking of pulmonary and other arteries by sickled cells. Sudden chest pain and other acute symptoms	Severe chest pain associated with dyspnea and features resembling pneumonia infection may supervene
Hysterical pain	Description of pain may vary from subject to subject and at different times in the same subject	Common symptom in hysterical subjects and malingeres

d. *Muscle pain:* Paroxysmal coughing may lead to rupture of muscle fibers which might present as superficial pain and local tenderness over the affected region of the chest wall. Movements aggravate the pain. Bornholm's disease caused by Coxsackie B virus causes severe muscular pain which may mimic pleurisy. It is accompanied by fever, malaise and headache.
e. *Costochondritis:* This common condition presents as dull localized pain and tenderness over the costochondral junctions. Chest movements, sneezing and coughing tend to aggravate pain.
f. *Rib fractures* present with history of sudden pain in the chest increasing with movement, respiration, coughing or sneezing. Fractures may result from trauma or pathological lesions such as secondary deposits or myeloma. Pathological fractures may be silent.
g. *Cardiac pain:* Chest pain is a prominent symptom in acute myocardial infarction, angina pectoris and pericarditis. Further details are given in Chapter 15.
h. *In mediastinitis* retrosternal pain may occur, varying in intensity. It is often accompanied by signs of infection such as fever and toxemia.
i. *Lesions of the aorta* such as aortitis and aneurysms give rise to dull aching pain in the retrosternal region. If the coronary arteries are involved the pain may resemble angina pectoris. In acute dissecting aneurysm of the aorta severe pain may be felt in the retrosternal region, with radiation along the major arteries to the neck, abdomen and down to the lower limbs.
j. Pain referred from the upper abdominal viscera might present as chest pain (e.g. pancreatitis, hepatitis and peptic ulcer) or as pain over the right shoulder, e.g. cholecystitis and liver abscess. Pain arising from lesions at the esophagogastric junction, such as peptic esophagitis and hiatus hernia, is usually localized to the epigastrium and retrosternal area. There may be a history of dysphagia to solids and liquids. The pain is felt as a retrosternal or epigastric burning sensation which increases after meals and is aggravated on bending forwards or lying in the supine position.
k. *Hysterical pain:* Chest pain may be a common symptom in hysterical subjects and malingerers. The descriptions may vary from subject to subject and at different times in the same subject. Distinction from other genuine causes may be difficult at times and may require prolonged observation and investigations.

Dyspnea (Table 12.4)

Dyspnea is defined as uncomfortable awareness of respiratory effort. Tachypnea is increased respiratory rate, the normal being 14 to 18/minute. Hyperpnea denotes increased volume of ventilation. Dyspnea occurs whenever the work of breathing is increased. Dyspnea may be due to diseases of bronchi, lungs, pleura or thoracic cage, cardiac failure, increased demand for oxygen, neurological diseases and psychogenic causes.

Types of Dyspnea in Various Respiratory Diseases

Upper airway obstruction: Dyspnea may occur acutely due to aspiration of food or foreign bodies which may block the larynx, or angioneurotic edema of glottis. Blocking of the larynx by large chunks of meat or other food materials during eating (cafe coronary) may present as sudden unconsciousness and respiratory arrest. The condition is fatal if the obstruction is not relieved as an emergency.

Tumors, or stenosis following tracheostomy can lead to obstruction. The hallmark of upper respiratory obstruction is the presence of stridor and inspiratory retraction of supraclavicular fossae.

Pulmonary parenchymal diseases: Pneumonia, extensive tuberculosis, bronchogenic carcinoma and interstitial lung diseases such as sarcoidosis and pneumoconiosis are common causes of dyspnea. There is tachypnea. The respiratory movements may be shallow. Respiratory failure may develop and this manifests as central cyanosis, mental confusion and flapping tremors.

Bronchial asthma: Acute intermittent obstruction with expiratory wheezing is typical of bronchial asthma. The attacks occur suddenly in paroxysms, especially worsened in the early hours of the morning. Several allergens like pollen or dust, environmental factors, respiratory infection and

Table 12.4: Pulmonary causes of dyspnea

Causes of acute dyspnea (within minutes)	*Suggestive findings*	*Risk factors*
Acute asthma	Episodic breathlessness and wheezing that arise spontaneously or after exposure to specific stimuli (e.g. allergen, URI, cold, exercise) and mental stress, bilateral rhonchi	Pre-existing history of reactive airway disease family history of asthma or atopy
Pneumothorax	Acute onset of sharp chest pain, tachypnea, diminished breath sounds, and hyperres-onance to percussion	Occur spontaneously in emphysema, COPD, and Marfan's syndrome, and following injury, and TB
Foreign body inhalation	Sudden onset of cough or stridor in a patient without URI or constitutional symptoms, Café coronary	Typically an infant or young child. Risk factors for aspiration in adults include alcoholism and anesthesia
Pulmonary embolism	Abrupt onset of sharp chest pain, tachypnea, and tachycardia	Cancer, immobilization, DVT, pregnancy, use of oral contraceptives or other estrogen-containing drugs, recent surgery or hospitalization
Toxic airway damage (e.g. inhalation of chlorine or hydrogen sulfide), burns	Sudden onset of suffocation and cough	Onset after occupational exposure or inappropriate use of cleaning agents
Cardiac causes		
Acute myocardial ischemia or infarction disease	Substernal chest pressure with or without radiation to the arm or jaw	Particularly in patients with risk factors for coronary artery disease (CAD) like hypertension, diabetes, obesity, hyperlipedemia and family history
Heart failure especially left heart failure, e.g. hypertension, ischemic heart disease, mitral stenosis, aortic valve disease	Dyspnea while lying flat (orthopnea) or appearing 1–2 hr after falling asleep (paroxysmal nocturnal dyspnea), crackles, S3 gallop, and signs of central or peripheral volume overload (e.g. elevated neck veins, peripheral edema)	Among patients with risk factors for Coronary artery disease (CAD)
Other causes		
Diaphragmatic paralysis and paralysis of other respiratory muscles	Frequent orthopnea	Sudden onset after trauma affecting the phrenic nerve. Following ascending paralysis
Anxiety disorder—hyperventilation	Situational dyspnea often accompanied by psychomotor agitation and paresthesias in the fingers or around the mouth	Normal examination findings and pulse oximetry measurements
Subacute (within days) or chronic breathlessness (weeks or months)		
Pneumonia	Fever, productive cough, dyspnea, sometimes pleuritic chest pain Focal lung findings, including crackles, decreased breath sounds, bronchial breath sounds and egophony	Children and elderly people
COPD exacerbation	Cough-productive or nonproductive, progressive breathlessness, accessory muscle use or pursed lip breathing, diminished air movement, bilateral rhonchi	Chronic smoker with smoking index >300. Exposure to indoor air pollution (biofuel mass)
Interstitial lung disease	Nonproductive cough and (progressive breathlessness. Clubbing and crakles on examination)	Occupational exposure to dust particles. (Extrinsic allergic alveolitis and collagen vascular diseases)
Asthma	History of pre-existing episodic breathlessness and wheezing that arise spontaneously or after exposure to specific stimuli (e.g. allergen, URI, cold, exercise) bilateral rhonchi	History of pre-existing reactive airway disease, family history of asthma or atopy

anxiety precipitate the attacks. Often the duration of dyspnea extends over several years. Family history of asthma and other atopic disorders may be present in many cases. Other allergic manifestations may coexist with asthma.

Chronic obstructive airway disease: In the initial phases of chronic bronchitis and emphysema, attacks of cough and wheezing develop during cold seasons (winter cough). These spells recur at shorter intervals and persist for longer periods as the disease progresses. Later dyspnea persists at all times with periodic exacerbations caused by infection or irritants.

Pulmonary embolism: The general pattern is that multiple small embolic episodes occur preceding a major embolus, which may be fatal in some cases. The minor episodes may be associated with acute dyspnea, chest pain and hemoptysis. In many cases the episodes are silent. A major attack comes on with sudden onset of severe dyspnea, cyanosis and loss of consciousness. Unless recognized early and promptly managed, the patient dies.

Pleural causes: Pleurisy, pleural effusion and pneumothorax commonly lead to dyspnea. Pneumothorax causes breathlessness of sudden onset. It may be severe and life-threatening in tension pneumothorax. As the intrapleural pressure increases the dyspnea worsens and this is a medical emergency. Pleural effusion may be associated with pleural pain and dyspnea. The dyspnea is more pronounced if the effusion collects rapidly and becomes massive. Chronic pleural effusions may even remain silent in some cases.

Diaphragmatic paralysis: Bilateral diaphragmatic paralysis leads to dyspnea. Transverse myelitis and demyelinating diseases such as Guillain-Barre syndrome may lead to diaphragmatic paralysis. Pressure on the phrenic nerves by tumors gives rise to uni-or bilateral paralysis. The patient is tachypneic. The abdominal wall is sucked in during inspiration and this is termed paradoxical respiration.

Diseases of the chest wall: Gross kyphoscoliosis and pectus excavatum which reduce the intrathoracic volume and distort intrathoracic structures give rise to dyspnea. The patient is tachypneic. Expansion of the chest is asymmetrical and non-uniform. Repeated respiratory infections and progressive changes in the lungs lead to the development of cor-pulmonale and respiratory failure.

Metabolic causes—acidosis: In metabolic acidosis caused by renal failure, diabetic ketoacidosis, prolonged starvation or poisoning by salicylates or methyl alcohol the respiration becomes deep and sighing in character. It is known as Kussmaul's breathing. The patient may or may not complain of respiratory discomfort.

Neurological disorders: In cerebral hemorrhage leading to coma, irregular and deep labored breathing may be present. Cheyne-Stokes respiration may occur in brain stem lesions.

Hysterical dyspnea: It is one of the frequent causes of dyspnea in those without systemic diseases. Dyspnea is more prominent at rest than during work. Exercise tolerance is often unimpaired. In extreme cases patient resorts to hyperventilation which produces dizziness, light headedness, tingling in fingers and even tetany as a result of respiratory alkalosis. Breathing returns to normal during sleep. Features suggestive of underlying anxiety or depression may be evident.

Abnormal Patterns of Respiration

Cheyne-Stokes Respiration (Fig. 12.1)

It is characterized by alternating periods of apnea lasting for 10 to 12 seconds, and hyperpnea. The breathing shows waxing and waning character. Breathing starts slowly at first, increases in rate and amplitude, and slows again to culminate in apnea. Cheyne-Stokes breathing is seen in cerebral hemorrhage, head injuries, poisoning, left ventricular failure, and chronic hypoxia. It may also occur in

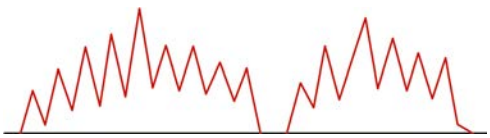


Fig. 12.1: Cheyne-stokes respiration

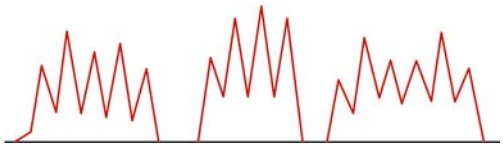


Fig. 12.2: Biot's respiration

normal persons at high altitudes, especially during sleep.

Biot's Respiration (Fig. 12.2)

It is seen mostly in brain damage and conditions such as meningitis. Here periods of apnea are interspersed with irregular deep breathing. Three to four respirations occur in clusters with apneic pauses in between. Unlike Cheyne-Stokes respiration, it has no waxing and waning character.

Sleep Apnea Syndrome

It is defined as cessation of breathing during sleep for at least 10 seconds. This can occur in normal subjects for up to ten times during rapid eye movement (REM) sleep every night. But if an individual has more than ten such apneic periods during a night's sleep, or more than 5 episodes during an hour he is said to have sleep apnea syndrome.

Sleep apnea is of two types:

1. Obstructive
2. Central.

Obstructive sleep apnea is associated with loud snoring in which harsh grunting inspiratory noise is produced. It is caused by transient total obstruction of the upper air passages. Obstruction may be due to marked obesity, enlarged tonsils and adenoids, or backward displacement of the tongue during sleep. The airflow stops while respiratory efforts continue as shown by abdominal and thoracic respiratory movements. In most of the cases the condition is benign. In severe cases the patients often show day time somnolence, morning headache, fatigue and personality changes like depression and hostility. Sleep apnea syndrome may be associated with increased risk of hypertension, cardiovascular disease and sudden death.

Central sleep apnea is due to a transient failure of respiratory drive. In this condition there is absence of respiratory movements along with cessation of air-flow.

Breath-holding in Infants and Children

Usually it occurs during the first four years of life. The child starts crying and stops breathing in the phase of expiration. Cyanosis develops around the lips. Breathing restarts after a gap. Some cases may develop convulsions and unconsciousness before the breathing restarts. Breath-holding can be physiological, or it may represent a psychological abnormality like anguish. Other causes include epilepsy and tetany.

Wheeze

These are musical sounds caused by partial obstruction of bronchial lumen, and this can be heard by the patients and others. The patient or his companions may complain of the wheeze. It is most commonly seen in bronchial asthma and other conditions where there is bronchial narrowing. In asthma this symptom occurs paroxysmally. When the bronchial obstruction is due to structural lesions, wheezing may be constant.

Stridor

Stridor is an inspiratory adventitious sound caused by obstruction to the large airways usually the larynx or trachea. A loud musical sound may accompany laryngeal spasm, e.g. inspiratory stridor in pertussis, laryngysmus stridulus in tetany, etc. Stridor may also be produced by tracheal stenosis or tumor.

Hoarseness of Voice

This is a common form of dysphonia. Dysphonia is abnormal alteration in phonation of voice sounds. It may result from several causes. Laryngeal lesions are most commonly accompanied by hoarseness. Simple laryngitis, and abuse of voice account for the majority. This condition is self-limiting. Mediastinal involvement by inflammatory lesions or neoplasms such as bronchogenic carcinoma with secondaries lead to hoarseness resulting from paralysis of the vocal cords. Retrosternal goiter may press upon the left recurrent laryngeal nerve and cause hoarseness. Dysphonia may also result from neurological disorders such as bulbar palsy or Parkinsonism. Total aphonia is usually hysterical.

PAST HISTORY

It is important to enquire about the past history of tuberculosis, pneumonia, allergies and asthma,

trauma to the chest, aspiration of foreign body or near-drowning, whooping cough, measles, anesthesia, surgery and seizures. Primary tuberculosis in early life may lead to lobar or segmental bronchiectasis later. Thoracic or upper abdominal surgery may be complicated by atelectasis (collapse) of the lungs. Patients who recover from near-drowning may develop aspiration pneumonia, atelectasis and lung abscess. Whooping cough may lead to bronchiectasis. Recurrent pneumonia may be a secondary complication of an underlying bronchiectasis or bronchogenic carcinoma.

Extensive bilateral tuberculosis can lead to massive pulmonary fibrosis and respiratory failure. History of BCG vaccination should be taken. BCG vaccination offers a good degree of protection from tuberculosis during childhood and adolescence. Immunity produced by BCG vaccination is only partial. This tends to wane off after 5 to 15 years. Since BCG vaccination is widely prevalent, it is a common cause of tuberculin positivity in childhood.

Patients presenting with pleural effusion may give a history suggestive of pneumonia or tuberculosis. Traumatic hemothorax may lead to gross pleural thickening. Sudden chest pain and dyspnea occurring in a patient convalescing from major surgery or acute illness requiring bed rest, may be due to pulmonary embolism.

History of Smoking Tobacco

Smoking is one of the most important risk factors for lung diseases, especially bronchogenic carcinoma and chronic bronchitis with emphysema. The ill-effects of tobacco smoking and the risk to health can be quantitated in terms of *smoking index*. Smoking index is the number of cigarettes smoked per day multiplied by the number of years of smoking. An index of over 300 makes a person highly prone to develop bronchogenic carcinoma. Smoking adversely affects other organ systems also. In places where *beedi* smoking is prevalent, four *beedies* may be equated to one cigarette. Smoking leads to aggravation of chronic bronchitis and bronchial asthma.

Occupational History

Inhalation of several dusts, gases, fumes and environmental pollutants can lead to lung diseases.

Table 12.5: Common occupational lung diseases

Coal dust	Anthracosis
Silica dust	Silicosis
Cotton dust	Byssinosis
Sugar cane dust	Bagassosis
Asbestos	Asbestosis, pleural mesotheliomas
Beryllium	Berylliosis
Isocyanates	Asthma
Wood dust, grain flour, vegetable dust	Asthma
Fungi in food products	Allergic alveolitis

The Table 12.5 shows some of the common occupational lung diseases seen in India.

Exact details of the duration of work, the amount of exposure, development of similar disease in fellow workmen, and familial tendency to develop such diseases, should be recorded.

Details of place of residence and hobbies should be enquired into. Individuals in close contact with parrots, pigeons or canaries are at risk to develop extrinsic allergic alveolitis or psittacosis. Atopic subjects when exposed to feathers, house dust, or animal dander may develop bronchial asthma or allergic rhinitis.

Family and Social History

Tuberculosis, chronic bronchitis with emphysema, respiratory allergy and asthma show strong familial predisposition. History of worm infestation in family members, especially in children, may give a clue to the origin of pulmonary eosinophilia. In Caucasian races cystic fibrosis of the lung is a frequent genetically determined disorder.

Cooking in closed environment with exposure to smoke from biofuels is a common cause of chronic bronchitis and emphysema in India.

History of Previous Treatment

A detailed history of past treatment of diseases such as allergies, asthma, pneumonia, tuberculosis and bronchitis should be taken. Previous radiographs if available, should be sought for comparison with present radiographs.

Noncompliance with treatment and failure to take the full course of antituberculosis treatment are major factors leading to problems such as development of drug resistance.

Several Drugs Cause Damage to Lungs

Methotrexate, busulphan, melphalan, bleomycin, mustine hydrochloride and similar antimitotic drugs may lead to pulmonary fibrosis. Weight reducing drugs such as fenfluramine and phenteramine used in the treatment of obesity lead to valvular diseases of the heart. Immuno-suppressive drugs such as corticosteroids, cyclophosphamide and azathioprine, predispose a person to exacerbation of tuberculous focus, viral infections, fungal infections such as candidiasis and aspergillosis and protozoal infections such as pneumocystis pneumonia. Similarly, acquired immunodeficiency syndrome (AIDS) is also associated with increased risk of all these infections.

PHYSICAL EXAMINATION

General Examination

1. *Attitude:* The effort for breathing is increased in dyspneic patients and the accessory muscles of respiration are more active. The patient prefers to sit in the propped up position leaning on a back rest.
2. *Mental state:* Hypoxia and carbon dioxide retention lead to restlessness, anxiety and confusion, flapping tremors, headache and signs of raised intracranial tension. Mental confusion, stupor and flapping tremors are suggestive of respiratory failure.
3. *Weight:* Recent loss of weight is common in pulmonary tuberculosis, tropical eosinophilia and bronchogenic carcinoma. Severe obesity causes dyspnea. Respiratory excursions of the chest and diaphragm are diminished in obese subjects. This predisposes to respiratory infections and respiratory failure.
4. *Flapping tremors:* These are suggestive of respiratory failure. These are elicited by making the patient hold his hands outstretched and they are then seen to flap irregularly, especially at the wrist joints. This is caused by dysfunction of the reticular formation in the brain.
5. *Fever:* It is common in respiratory infections such as pneumonia, tuberculosis and pleurisy.
6. *Anemia:* It may be caused by severe hemoptysis. Pulmonary tuberculosis may be associated with malnutrition and anemia.
7. *Cyanosis:* Respiratory failure leads to central cyanosis. Longstanding chronic respiratory failure leads to secondary polycythemia which further aggravates the cyanosis.
8. *Lymphadenopathy:* Lymph node enlargement may be seen commonly in pulmonary tuberculosis, carcinoma, sarcoidosis and lymphomas. Supraclavicular, scalene, cervical and axillary nodes should be carefully palpated to detect early lymph node enlargement. Mediastinal lymph node enlargement is commonly secondary to bronchogenic carcinoma, sarcoidosis, lymphomas and primary tuberculosis. Enlarged lymph nodes in bronchogenic carcinoma and lymphomas may lead on to mediastinal obstruction.
9. *Clubbing of fingers:* Bronchiectasis, lung abscess, bronchogenic carcinoma, chronic pulmonary tuberculosis, empyema (collection of pus in pleural cavity) and pulmonary interstitial fibrosis lead to clubbing of fingers. Grade four clubbing is suggestive of longstanding suppurative lesions such as bronchiectasis, lung abscess, and empyema (Fig. 12.3).

 Pulmonary osteoarthropathy is the condition where there is painful clubbing, thickening of the periosteum of the distal parts of the radius, ulna, tibia and fibula and painful enlargement of ankles and wrists. This may develop in bronchogenic carcinoma and less commonly, in chronic suppurative lesions.
10. *Edema:* This may be caused by right sided heart failure which may complicate chronic pulmonary diseases such as chronic bronchitis emphysema and pulmonary fibrosis. Development of right ventricular enlargement and/or right sided heart failure secondary to pulmonary diseases is termed cor pulmonale.



Fig. 12.3: Clubbing of fingers

11. *Jugular veins:* With patient recumbent at 45°, the internal jugular veins are examined for abnormalities. Elevation of jugular venous pressure (JVP) may point to pulmonary heart disease, i.e. cor pulmonale. Other signs to be looked for include tender hepatomegaly, dependent edema, and ascites (for further details see Chapter 2). In asthmatic patients filling of jugular veins during expiration and emptying during inspiration may be noticed.

Respiratory System Examination

Nose, paranasal sinuses, ears and throat should be examined before proceeding to the chest (See Chapters 52 and 53).

Movement of Accessory Muscles

When there is respiratory distress as in chronic obstructive airway disease and bronchial asthma, accessory muscles come into play.

1. Sternomastoids, scaleni and trapezius become prominent during inspiration.
2. Abnormal recession of supraclavicular and suprasternal fossae during inspiration indicates excessive inspiratory effort. Yet another feature suggesting increased respiratory effort is the flare of the nostrils due to the action of alae nasi.

Nose and Throat

The nose, paranasal sinuses and the throat should be examined. Examination of throat may reveal congestion and enlargement of adenoids and tonsils, which may be related to pulmonary disease. When indicated, laryngoscopic examination may have to be done to detect tuberculous ulceration in larynx, carcinoma and paralysis of vocal cords (for details see Chapter 51).

Examination of the Neck

Neck should be examined for:

i. Posture
ii. Movements of accessory muscles
iii. Jugular veins
iv. Position of the trachea
v. Abnormalities of the lymph nodes and thyroid, and
vi. Other abnormalities if any.

Inspect the position of the trachea and its movement with respiration. Normal trachea is in the midline. Tracheal shift may be caused by pulmonary and pleural lesions. Pulmonary fibrosis and collapse pull the trachea towards the side of lesion while pneumothorax and pleural effusion push the trachea to the opposite side.

Local lesions in the neck such as thyroid mass and lymphadenopathy also displace the trachea. In kyphoscoliosis involving cervicodorsal regions of the spine there is apparent shift of the trachea.

Examination of cervical lymph nodes and thyroid are described in Chapters 2 and 26.

Examination of Chest

The procedure for examining the chest includes inspection, palpation, percussion and auscultation.

Inspection

The chest should be examined in good light, with the patient preferably sitting up, the body exposed down to the waist. Systematically observe the front, back and also from above downwards by looking over the shoulders. In the acutely ill and recumbent patient, the chest should be inspected from the foot end of the bed towards the neck and from the head end of the bed over the clavicles. Normally the trachea does not move visibly during respiration. Inspiratory indrawing of the trachea is caused by increased respiratory effort as seen in emphysema and tracheal obstruction. Movement of the trachea from side-to-side may occur in fibrosis of the upper lobes.

For purposes of description and recording of abnormal findings, the chest is divided into nine regions as described in Chapter 11.

Presence of abnormal findings over different regions of the chest helps to localize the lesion to the underlying portions of the lungs.

Shape of the Chest

Normally the anteroposterior diameter is less than the transverse diameter. Changes which occur in the chest with ageing include increasing kyphosis of the dorsal spine, increase in anteroposterior length of the chest and diminution in the amplitude of respiratory movements. If these changes occur in the young or in the middle aged, they are likely to be due to emphysema.

Alteration in the Physical State of the Lungs in Disease

Before proceeding further to examine the respiratory system, the student should get familiarized with physical alterations that take place in the lungs and pleura as a result of disease. These are responsible for the abnormal physical findings on examination. Normal lung is soft, air containing, sponge like and capable of full aeration. The air passages do not contain secretions in excess.

Consolidation

This term refers to the state of the lung in which, due to inflammatory or neoplastic processes, the lung assumes the physical state of a solid organ. The consolidated area does not contain air, does not take part in ventilation and does not change in volume from the normal. It becomes more conductive to sounds and vibrations, and therefore the bronchial sounds and vibrations of the vocal cords are easily transmitted to the chest wall.

Collapse/atelectasis: The lung becomes shrunken due to loss of air, either due to obstruction to bronchial lumen or pressure from outside.

Fibrosis: The lung tissue is replaced by fibrous tissue which may be the result of inflammatory processes. The volume is reduced and the texture is altered. Ventilation does not take place.

Cavitation: The lung tissue is destroyed by suppurative or neoplastic processes and the necrotic material is coughed out, leaving behind cavities of different sizes. These may be empty, partially filled with material or full. They may communicate with a bronchus or remain closed.

Emphysema: The alveoli become overdistended and the residual volume is increased. Since the lung tissue loses its elasticity, expiration is not complete. Normal ventilatory excursions are considerably reduced. Emphysematous lung does not conduct vibrations to the chest wall as efficiently as normal.

Pleural effusion: Fluid collects in the pleural cavity. This leads to collapse of the lung and also prevents its expansion. Vibrations and sounds are blocked at the air-fluid interphase.

Pneumothorax: Air enters the pleural cavity. The negative pressure in the pleura is abolished. The lung collapses towards the hilum by its own recoil and it does not take part in ventilation. Pneumothorax may be complete or partial.

In tension, pneumothorax air collects inside the pleural cavity under pressure, compresses the lung and pushes the mediastinum to the opposite side.

Deformities of the Chest

Shape of the chest may be altered in several conditions:

1. Respiratory obstruction and adenoids, (see Chapter 51).
2. Rickets.

 The usual abnormalities that may be associated with rickets are pigeon chest, Harrison's sulci and rickety rosary. Pigeon chest (Syn: Pectus carinatum) is seen usually in rickets and also in asthmatic children. It is characterized by marked protrusion of sternum and adjacent costal cartilages.

 Harrison's sulcus is a groove running laterally from either side of the sternum along the lower ribs, caused by pull at the attachment of the diaphragm.

 Rickety rosary is characterized by bead-like enlargement of costochondral junctions.
3. Congenital disorders of vertebral column like kyphoscoliosis and pectus exacavatum and acquired diseases such as tuberculosis, osteoporosis and ankylosing spondylitis lead to deformity.

 Pectus excavatum (Syn: Funnel breast, cobbler's breast): This is often congenital in origin. It is characterized by marked exaggeration of normal hollow over the lower end of sternum. Sometimes it is seen in cobblers, because of constant pressure of shoes against the lower part of sternum.

 When the deformity is severe the thoracic cavity is encroached upon and this results in pulmonary and cardiovascular complications.
4. Diseases of underlying lungs like chronic obstructive airway disease, pleural effusion, pneumothorax, collapse and fibrosis result in visible abnormalities.

Barrel shaped chest: The chest is held in inspiratory position, with ribs held more horizontally, and anteroposterior diameter is increased. This is seen in emphysema.

While inspecting the chest, one should look for unilateral bulging, flattening or retraction which may be localized to one area or involve a whole side. Unilateral bulging and widening of rib spaces may be seen in pleural effusion, pneumothorax, and compensatory emphysema. Precordial bulge may be caused by gross cardiomegaly developing in early life, pericardial effusion and aortic aneurysm. Malignant disease of chest wall, mediastinum or lungs, local diseases of ribs and sternum, and spinal deformities lead to localized bulge on the chest wall. Pulmonary collapse and fibrosis leads to localized retraction and crowding of the ribs. Wasting and retraction are particularly seen below the clavicle and the upper part of the trapezius in apical pulmonary tuberculosis.

Drooping of shoulders: The patient should be examined from the front while he is standing and breathing normally. In apical fibrosis or collapse of the upper lobes, the ipsilateral shoulder droops, i.e. it is at a lower level than the other.

Dilated veins on the chest: In mediastinal obstruction the jugular veins, and veins over the upper part of the chest become distended and enlarged. In this condition the jugular veins do not show normal pulsation. In inferior vena caval obstruction veins from the abdomen may be seen to run upwards over the chest wall, with blood flowing upwards.

Respiratory Rate

The resting respiratory rate in adults is 16 to 20 per minute. The pulse to respiration ratio is 4:1. It is important to look for respiratory rate without drawing the attention of the patient since awareness tends to make respiration irregular. The best way to avoid this is to note the respiratory rate while apparently counting the pulse. Respiratory rate is higher in children. It is increased in nervous subjects, fever, acute pulmonary infections, obstructive airway disease, high altitudes and acute pulmonary edema. Increase in respiratory rate is called tachypnoea. The respiratory rate is lowered in narcotic poisoning (e.g. morphine), some forms of respiratory failure, raised intracranial tension and head injury.

Types of Breathing

In children and men diaphragmatic action is more prominent. The downward movement of diaphragm during inspiration causes the abdominal wall to bulge forwards. During expiration the abdominal wall recedes. This type of respiration is termed abdominal respiration. In contrast, in women, action of the intercostal muscles is more prominent and then respiration is mainly thoracic. The pattern of respiratory movements may change in several diseases. In conditions where diaphragmatic movements are restricted because of pain, as occurring in liver abscess, the respiration becomes thoracic. Conversely, in conditions where the chest movements are restricted as in pleurisy, the respiration becomes abdominal. During advanced pregnancy respiratory movements are mainly thoracic.

Depth of respiration should be observed. In conditions like diabetic coma, and uraemia, which lead to metabolic acidosis, the depth of respiration is strikingly increased and expiration may be accompanied by a quiet hissing noise. This is called Kussmaul's respiration. Other causes of deep respiration are anxiety, exercise, fever, and thyrotoxicosis. Sighing respiration is seen in hysterical subjects. It should be realised that the depth of respiration has hardly any direct correlation with the efficacy of alveolar ventilation.

Respiration becomes shallow in conditions when respiratory movements are impaired by muscular weakness and painful conditions in the chest, like pleurisy or local injury. During sleep respiratory movements tend to be shallow. In central respiratory depression caused by narcotic poisoning and brainstem disease the breathing is shallow.

Paradoxical movements: These occur when there is diaphragmatic paralysis. Unlike as in the normal, during inspiration the abdominal wall is sucked in and vice versa *paradoxical breathing*.

Flail chest movement: This happens in traumatic lesions when a portion of the chest wall gets detached from the thoracic cage due to multiple fractures of

ribs. During inspiration, this part of the chest is sucked in, thereby preventing expansion of the lungs.

Expansile impulse on coughing: Development of an expansile bulge on coughing indicates the presence of a fistulous communication between the pleural cavity and the subcutaneous plane in the chest wall. This may develop as a complication of empyema and it is known as empyema necessitans.

Position of apex beat and trachea: Displacement of the apex beat and the trachea may be caused by displacement of the mediastinum towards the side of lesion as in fibrosis or collapse of the lung, and away from it in pleural effusion and pneumothorax.

Skin over the chest wall: It should be examined with a view to detect subcutaneous nodules in malignancy; also for marks of puncture, incision, and scars.

Palpation

Before commencing palpation of the chest ascertain: (1) Position of the trachea and apex beat and (2) Presence of lymph node enlargement.

Palpation of the Trachea

The patient's neck is slightly flexed without rotating the head, and trachea is palpated above the suprasternal notch. Normally it lies in the midline equidistant from the origin of each sternomastoid muscle, or it may be slightly deviated to the right (Fig. 12.4).

Apex beat: Normally apex beat is felt as a thrust in the fifth left intercostal space 1.5 cm medial to the midclavicular line (See Chapter 15).

Palpation of the Chest

Localized tenderness over the chest may occur in rib fractures, trauma, secondary deposits, herpes zoster, pleurisy, costochondritis and other affections of the ribs, sternum or intercostal muscles.

Expansion of the Chest

Normally the chest expands 5 to 7 cm in an adult male and 5 to 6 cm in an adult female. Expansion should be recorded using a measuring tape. Expansion of each hemithorax can be measured by holding the tape from the vertebral spine to the mid point of the sternum. *Since this is a very reliable and reproducible method, the inspiratory and expiratory measurement of the chest at the level of the third costochondral junctions should be recorded in all cases.*



Fig. 12.4: Palpation of the trachea—the middle finger locating the trachea in relation to the midline

Expansion of the chest decreases with age. In emphysema, pleural effusion and pneumothorax, the affected side is prominent and expansion is diminished. In collapse and fibrosis, the lung on the affected side is shrunken and movements are diminished. In ankylosing spondylitis the expansion is diminished or abolished.

Comparison of movements of both sides of the chest should begin with upper lobes. The examiner should stand behind the patient, looking over the patient's shoulders and place the hands over both the suprascapular regions. For comparison of the infraclavicular regions and infra-axillary regions the palms of the hands are applied tightly over the corresponding area on either side. The hands are placed symmetrically so that the thumbs just meet in the midline over the sternum on full expiration and are held loosely. Movement is assessed by noting the excursion of the thumbs from the midline and the feel over the palms (Fig. 12.5).

Palpate the: (1) supraclavicular region, (2) infraclavicular region, (3) axilla, (4) supra-scapular region, (5) interscapular region and (6) infrascapular region.



Fig. 12.5: Palpation of the chest for movement. *Note:* The palms of the examiner are firmly applied to the part to be examined. The thumbs act as pointers transmitting the movement

Diminution of movements can be both felt and seen.

Minor differences in movements are not uncommon and may occur in health. Obvious asymmetry denotes disease of the underlying lung.

The important causes of diminution of movement are consolidation, pleural effusion, pneumothorax, emphysema, collapse and fibrosis. When both sides are diseased, the expansion as a whole may be reduced. The examiner should gain sufficient experience to assess normal movements so that uniform reduction in expansion of both sides can be recognized.

Rhonchial Fremitus

These are palpable rhonchi.

Pleural rubs may be palpated at times. Other palpable abnormalities include crepitus in surgical emphysema, ends of broken ribs and flail chest.

Vocal Fremitus

This is the vibration transmitted to chest wall from vocal cords on speaking. These vibrations from the larynx are transmitted to the chest wall by the larger air passages and lung.

Method: Place the palm or the ulnar border of the hand on the patient's chest when he is made to say "one, two, three", or "ninety-nine" in local language. Corresponding areas on the chest are compared for the intensity of vocal fremitus. In thin subjects vocal fremitus will be more prominent, and in obese subjects it will be diminished.

Vocal fremitus is altered in pulmonary and pleural diseases. It will be decreased when transmission of vibrations is impaired, e.g. bronchial obstruction, pleural effusion, pleural thickening or pneumothorax and emphysema.

Vocal fremitus is increased in conditions where the lung assumes the texture of a solid organ as in pneumonic consolidation and neoplasms, or when a collapsed segment of the lung lies in direct contact with a bronchus or trachea.

Percussion of the Chest

Percussion involves the setting up of vibrations in the underlying tissues with a sharp tap using the fingers. Percussion over the chest is done to determine the state of the underlying lung and pleura, and to demarcate the borders of the lungs and heart. It is done by placing a finger, usually the left middle one, firmly on the chest wall (pleximeter finger) and striking the distal part of middle phalanx with the tip of the right middle finger (plexor finger). The intercostal spaces on either side are percussed symmetrically. The examiner should get sufficient experience to appreciate normal percussion notes over different areas of the chest so that any alteration in disease can be appreciated (Fig. 12.6). Percussion notes over different areas of the chest differ depending on the volume of underlying lung.

When percussing over bones (e.g. clavicle), direct percussion is done without the pleximeter. Points to be elicited by percussion are: (1) The note which is produced and (2) the sensation of resistance and vibrations imparted to the pleximeter and plexor fingers. Percussion note over chest has to be learnt by practice.

Beginners Make Three Common Mistakes

1. The percussed finger is kept loosely on the chest wall.
2. The percussing finger and wrist are held stiff. It is necessary that the examiner applies the pleximeter finger firmly to the chest wall. The stroke must be sudden, delivered by the flexion of the wrist and the striking finger should be



Fig. 12.6: Percussion of the chest. Arrow points to the plexi meter finger placed on the chest. Arrowhead points to the plexor finger

withdrawn immediately after the stroke so as to avoid dampening of resulting vibrations.

3. Unless specifically indicated, percussion should be gentle, since it is the quality of the note and not its intensity alone that is diagnostic. Heavy percussion by the beginner may cause pain and this leads to resentment from the patient and also may worsen the condition if there is hemoptysis.

While percussing over lungs one should compare corresponding areas on both sides. For percussing the back, the patient is made to sit up with his arms held across the chest so as to move the scapulae laterally and expose a greater part of the thoracic cage.

Percussion notes are described as resonant, hyper-resonant, tympanic, dull and stony dull or flat.

Resonant note: This is the note obtained over normal lung tissue. It has a distinctive and clear character with a low pitch. Areas below clavicles and scapulae are more resonant because of greater volume of underlying lung tissue and relative lack of musculature, while the other areas are less resonant.

Abnormal Percussion Notes

These are increased resonance:

1. Hyper-resonant,
2. Tympanic (also termed tympanitic).
3. Decreased resonance:
 a. Impaired
 b. Dull
 c. Stony dull (flat).

Hyper-resonant note: Increased or excessive resonance is elicited in conditions where lungs are over distended as in emphysema or when there is free air in the pleural cavity as in pneumothorax.

Tympanic: As its name implies, this is an extreme form of hyper-resonant note. This "drum-like" note is heard over viscera which contain gas without loculation, e.g. in stomach, or intestine. Percussion note over a large superficial cavity in lung or pneumothorax is tympanic.

Impaired percussion note: This is obtained when the underlying lung becomes comparatively airless as is seen in consolidation, collapse and fibrosis. In all these conditions, the underlying pathological lesion is surrounded by normal lung tissue, and hence the note is only impaired.

Dullness: The percussion more resembles that obtained over a solid organ such as the liver. It is seen in pulmonary collapse, consolidation, and pleural thickening.

Stony dull note (Syn: flat note): Stony dullness resembles the percussion note over the thigh. It is found over pleural effusions, and in large growths in the lung or pleura.

Cardiac dullness: The portion of the chest overlying the heart can be mapped on the chest anteriorly by gentle percussion starting from the resonant area and moving towards the cardiac borders. First the upper border of the liver dullness is defined by percussion. The right border can be identified by percussion starting from the right of the sternum keeping the plexi meter finger parallel to the right border of the heart and moving towards the left. Similarly, the left border of heart can be defined by percussion starting from the left axilla and moving towards the right. Figure 12.7 shows percussing of upper border of liver.

Normal Borders of Cardiac Dullness

(See also Chapter 15, percussion of the precordium) Right border is formed by the right atrium, and it is in the right lateral sternal line. Left border is formed



Fig. 12.7: Defining the upper border of the liver by percussion. Note that the pleximeter finger is placed parallel to the upper border of the liver in the third Intercostal space and progressively brought down

for the most part by the outer border of the left ventricle and it is in line with apex beat. Upper border is formed by the aorta and pulmonary artery and it is at the level of the second intercostal space behind the sternum. The lower border cannot be separately percussed out since it is continuous with the dullness produced by the liver. Cardiac dullness is obliterated if overdistended lungs encroach on the bare area of the heart. This happens in emphysema. The area of cardiac dullness is increased in pericardial effusion and cardiomegaly.

Upper border of a pleural effusion can be defined by percussing from above downwards. In simple pleural effusion the dullness is higher in the axillae than in front and back. This phenomenon of rise of the level of the dullness in the axilla compared to the front and back is termed Ellis' "S" shaped curve. Fluid in the pleural cavity causes the lung to collapse towards the hilum. The part of lung below the hilum is fixed by pulmonary ligament and as a result, the fluid tends to rise in axilla.

On percussing with the same force it will be seen that the note is "stony dull" in the lower parts, while in the higher regions the note has impaired resonance.

When the pleural cavity contains air and fluid and upper border of fluid is straight and horizontal. Change in posture results in shift of position of the fluid. This phenomenon can be demonstrated by eliciting shifting dullness. Chest is percussed with the patient sitting up and the upper border of the dullness is demarcated. The horizontal level of dullness can be clearly distinguished from the hyper-resonance of the air above. The patient is then made to lie down without changing the position of the pleximeter finger. After waiting for 10 seconds for the fluid to move, percussion is repeated. The previously dull area becomes resonant, since the fluid gives place to air.

Tidal Percussion

This method is employed to distinguish whether the cause of dullness over the lower part of the chest is due to upward enlargement of liver or spleen, or due to an intrathoracic pathology. The technique is to percuss the lower part of the chest to mark the level of dullness twice: (i) at the end of deep inspiration and (ii) again at the end of deep expiration. The difference in the level of lung resonance gives an indication of range of movement of the diaphragm. In intrathoracic causes the dullness does not shift with inspiration whereas in subdiaphragmatic causes it does go down. It should be borne in mind that in painful lesions such as amoebic abscess of the liver, the diaphragm may not move down fully.

Cracked pot sound: This is the percussion note sometimes elicited over cavities which communicate with the bronchus. It resembles percussion over a cracked pot.

Auscultation of the Chest

The patient should breathe normally and the examiner should systematically auscultate at all lung areas with the stethoscope.

Auscultation is performed to bring out the following points: breath sounds, added sounds, vocal resonance, bronchophony, egophony, whispering pectoriloquy and other special forms of auscultation.

Breath Sounds

Intensity of breath sounds (Fig. 12.8) should be noted. The intensity decreases if an area of the lung is not ventilated properly or the chest wall is very thick as in obesity. Decreased intensity is seen

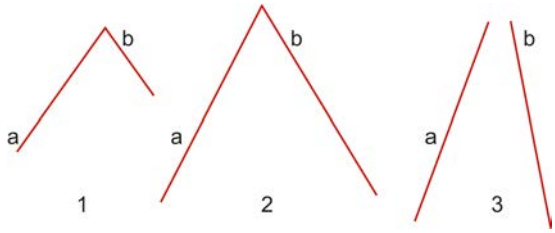


Fig. 12.8: Breath sounds (1) Vesicular breathing, (2) Bronchovesicular breathing, (3) Bronchial breathing (a) Inspiratory phase (b) Expiratory phase

pathologically in collapse, fibrosis, pleural effusion, pneumothorax, thickened pleura and in obstruction to a bronchus. In severe emphysema and acute severe asthma breath sounds are diminished. In central respiratory depression the rate and depth of respiration go down. In respiratory paralysis, respiration becomes weak and shallow.

In children the breath sounds are louder and harsh. They are called *puerile breath sounds.* Breath sounds may be vesicular or bronchial

Vesicular breath sound: It is produced by the passage of air in the air passage and modified by the movement of the alveoli. It is low-pitched and characteristically described as rustling (Rustle denotes a sound produced by blowing air on dry leaves). The sound of expiration closely follows the inspiration without a pause, and the duration of expiration sound is only half that of inspiration.

Bronchial breath sound: It is produced by passage of air through the trachea and large bronchi. It is normally audible over the trachea. Bronchial breath sound is characterized by the presence of a gap between inspiration and expiration; expiratory phase equals the inspiratory phase. These sounds are also hollow in character.

Bronchial breath sound can be further divided into three types:

i. *Tubular breath sound:* This sound is deep hollow and high pitched in character and it closely resembles the sound produced by blowing into a hollow tube. It is characteristically seen in pneumonic consolidation and in some cases of collapse with a patent bronchus.
ii. *Cavernous breath sound:* Cavernous breath sound is low pitched bronchial breath sound. There are no high pitched overtones. It is heard over cavities which are empty and which communicate with a patent bronchus. The breath sounds heard on direct auscultation of the trachea or behind the neck are low pitched bronchial in character.
iii. *Amphoric breath sound:* Amphoric breathing is a low pitched bronchial breathing with high pitched overtones, which give the sounds a metallic character. It resembles the sound produced by blowing across the narrow neck of a bottle. This sound is heard in open pneumothorax and over large cavities communicating with a bronchus.

Bronchovesicular breath sound: In this type of breath sound the duration of expiration and inspiration are equal and there is no pause between them. This may be heard over normal lungs, especially over the right infraclavicular region.

Prolongation of Expiratory Phase

This occurs in bronchial asthma and obstructive airway disease. Often the character of the expiratory phase is altered and wheezing may be present.

Added Sounds (Syn: Adventitious Sounds)

These may arise from the lung, pleura or the chest wall. Sounds caused by friction between the skin and stethoscope should be avoided by placing the stethoscope firmly on the chest wall.

a. *Wheezes and rhonchi:* Wheezes are musical lung sounds heard at a distance near an asthmatic patient. When heard by auscultation they are termed rhonchi.

These are whistling sounds, which are produced by partial blockade of bronchi. Partial obstruction leads to turbulent airflow which produces the wheeze. Wheeze does not occur if the lumen is fully patent or severely narrowed. Spasm of bronchial muscles, mucosal swelling and presence of thick mucus lead to bronchial obstruction.

Rhonchi may be high pitched (sibilant) or low pitched (sonorous) depending on the size of the bronchi of origin; they may be heard collectively (polyphonic). In bronchial asthma and chronic bronchitis, they are audible over all areas and are present during expiration and inspiration, generally more prominent during

expiration. Localised rhonchi should suggest the possibility of bronchial obstruction due to secretions, carcinoma, lymph nodes or a foreign body. In diffuse interstitial pulmonary fibrosis inspiratory wheezes may be heard over the lower parts of the chest.

b. *Crackles (Syn: crepitations):* Interrupted bubbling or crackling sounds are called crepitations or *rales*. They are of two types:
 1. *Fine crepitations:* Mostly these are inspiratory and are produced by sudden opening of intrapulmonary airways which are apposed during expiration. They are heard in the early stages of pneumonia and in heart failure.
 2. *Coarse crepitations:* These are produced by the movement of air through small and medium air passages which are filled with fluid and the sudden opening of relatively stiff alveoli as in fibrosing alveolitis.

 Sometimes, crepitations may be heard over the dependent parts of lungs after prolonged recumbency, even in the absence of disease. These disappear on coughing. Crepitations that persist even after coughing, and those which appear or increase with coughing should suggest pathological lesions. In conditions like tuberculous cavities, lung abscess, and other inflammatory lesions, crepitations become more prominent after coughing (post-tussive crepitations).
c. *Pleural friction rub:* It is a superficial, leather-creaking sound heard when the pleura is thickened as in inflammation, malignancy or infarction. It is heard during the same phases of the respiratory cycle, often during both inspiration and expiration. It is not altered by coughing.
d. *Pleuropericardial sounds:* If pleurisy and pericarditis coexist, pleuropericardial rub may be heard when the lungs come into more intimate contact with the pericardium in inspiration. The hallmark of pleuropericardial friction is accentuation when the breath is held in inspiration. Sometimes friction rub may be heard over a wider area and may not be limited to the precordium.
e. *Crunching sounds:* These may be heard while auscultating over areas of surgical emphysema, and sometimes over pericarditis.
f. *Knocks:* Sharp adventitious sounds may be produced by movement of the collapsed lung against the mediastinum on the side of a pneumothorax. At times pericardial knocks may be heard.

Vocal Resonance

The mechanism of production of vocal fremitus and the method to elicit it have been described. The same laryngeal vibrations can be auscultated over the chest wall. The patient is asked to repeat syllables like "one, two, three" or "ninety-nine" (in local language) and the intensity and character of these sounds are compared over corresponding areas of the chest on both sides. The examiner should get an idea of the normal intensity of vocal resonance in thin and stout individuals by practice. Increased vocal resonance is known as *bronchophony.* This is heard over areas of consolidation. Vocal resonance is decreased or absent in pleural effusion and in pneumothorax.

If the sounds are heard clearly and syllables can be made out distinctly it is known as *pectoriloquy.* Pectoriloquy obtained when the patient whispers is known as *whispering pectoriloquy*. This is present generally over areas where bronchial breathing is present, such as consolidation, cavities communicating with bronchi and others.

In some cases of pleural effusion, above the level of effusion, the vocal resonance may be high pitched with a characteristic nasal quality. This is called egophony.

Special Procedures in Auscultation

Succussion splash: This is a splashing sound which can be auscultated (even palpated at times) over a hydropneumothorax or a large superficial cavity containing air and fluid. While auscultating over the upper level of fluid, the patient is shaken from side-to-side and the splash of fluid can be heard. Presence of succussion splash is a definite evidence of presence of fluid and air in a cavity.

Post-tussive suction: This is a sucking noise produced when air rushes into a thin walled collapsed

cavity during inspiration. It is generally heard over superficial empty cavities communicating with bronchi.

Method: While auscultating, the patient is made to cough. Post-tussive suction is heard during the inspiration that follows.

Post-tussive suction and post-tussive crepitations strongly suggest the presence of cavitating lesions in the lung. Thick walled cavities such as lung abscess and cavitating tumors do not collapse with coughing and therefore post-tussive suction may not be present in them. Tuberculous cavities commonly give rise to this sign.

Coin sound: This is a special auscultatory sign which can be elicited over areas containing free air, such as pneumothorax, large pulmonary cysts, and bullous emphysema. The chest is percussed at the back or front using two coins (one acting as the pleximeter and the other as the plexor) and the examiner auscultates from the opposite side. Normally the lungs do not transmit the ringing metallic sounds distinctly. When there is free air between the areas, the sounds are heard with a ringing metallic quality.

Sputum

After completing the physical examination, special enquiry should be made regarding the quantity and nature of sputum. A specimen of fresh sputum should be observed and taken for further examination.

A Scheme for Recording Physical Findings in the Respiratory System (Table 12.6)

Upper Respiratory Tract

Nose: Nostrils, nasal septum, sinuses

Mouth: Mucous membrane, teeth, tongue

Throat: Normal, congested, tonsils other abnormalities

Table 12.6: Recording of findings in respiratory system

Variable	*Outcome*
Swallowing	Normal, abnormal
Respiratory rate/minute	
Type of respiration	
If abnormal, details	
Accessory muscles	Overactive/normal
Alae nasi	Normal/overactive
Trachea	Central, shifted to one side
Respiratory retraction	
Jugular veins	Normal, engorged, inspiratory emptying.
Chest inspection shape	Normal-abnormal Localized flattening Retraction-bulging
Movements	Normal-increased, decreased
Palpation trachea	Central-shifted to–
Apex beat	Normal-shifted to–
Tenderness over chest	Present-nil
Expansion of chest	Measurement
Localized diminution of expansion	expiration, inspiration Details
Vocal fremitus	Normal, increased, decreased
Rhonchial fremitus	Present, absent
Palpable rub	Present, absent
Percussion	Normal note impaired note, dull note, stony dull note hyper-resonant note
Upper border of liver	
Cardiac margins	Right, left

Contd...

Contd...

Variable	*Outcome*
Auscultation	
Breath sounds	-
Intensity	Normal Reduced Increased
Type of breathing	Normal-(vesicular) Bronchial
If bronchial type	Tubular, cavernous, amphoric
Added sounds	Present Absent
Rhonchi if present	Sibilant, sonorous
Crepitations	Present Absent
If present	Fine, coarse, others
Effect of coughing	Disappears, Remain the same, Increase
Pleural friction rub	Present-absent
Other adventitious sounds if any	Present-absent
Vocal resonance	Normal, increased, decreased
Whispering Pectoriloquy	Absent-present
Special physical findings	
Upper border of dullness to percussion if pleural effusion is suspected	Front, axilla, back
Shifting dullness	Present-absent
Coin sound	Present-absent
Local bulge with expansile impulse on Coughing	Present-absent If present, details-nil
Sputum	Normal amount only, increased. If increased, quality and character
Abnormality of sputum	Purulent-watery-foul smelling-blood stained others

Interpretation of Physical Findings

A few examples of the common abnormalities are given below:

Problem

Find out the probable physical diagnosis.

Case 1

Male aged 30 years—fever, chest pain on the right side, dyspnea for 3 days.

- Respiratory rate 30/minute
- Trachea is central
- Apex beat in the 5th left intercostal space inside the midclavicular line
- Shape of chest—normal
- Movements of the chest are diminished in the upper part on right side
- Vocal fremitus is increased over the right infraclavicular region
- Percussion note is dull in this area
- Breath sounds are bronchial in character
- Fine crepitations are present
- Whispering pectoriloquy is present

Diagnosis: Pulmonary consolidation right upper lobe pneumonia.

Case 2

Male aged 50 years—Fever, pain right side of chest and dyspnea 3 weeks.

- Respiratory rate 30/minute
- Trachea is shifted towards left
- Apex beat is seen 2 cm, outside the left mid-clavicular line in the fifth space
- Right side of the chest is prominent and bulging
- Movements of right side of chest are diminished
- Vocal fremitus is decreased on the right side of the chest both in front and back
- Percussion note is stony dull below the third rib in front and seventh dorsal spine behind dullness rises in the axilla
- Intensity of breath sounds is markedly diminished

- There are no added sounds
- Vocal resonance is decreased

Diagnosis: Pleural effusion right side.

Note: In pneumothorax, all physical findings are usually similar to that of pleural effusion except that the percussion note is hyper-resonant on the affected side. In pleural thickening mediastinal shift may not be present and the affected side may not be bulging.

In later stages, the affected side may actually retract due to fibrosis.

Case 3

Male 30 years—dyspnea and cough following near drowning 3 days ago.

- Position of the trachea is shifted to the right side
- There is flattening of the right infraclavicular region. Right shoulder is drooping
- Movements of the chest are diminished in this region
- Vocal fremitus is diminished
- Percussion note is dull
- Breath sounds are absent
- Vocal resonance is diminished
- There are no added sounds.

Diagnosis: Collapse right upper lobe due to obstruction of right upper lobe main bronchus.

Case 4

Woman aged 50 years with a past history of pulmonary tuberculosis, has chronic cough for 5 years and occasional hemoptysis.

- Retraction on the right side of chest, right shoulder is drooping. Trachea is shifted to the right. Apex beat is not felt distinctly.
- Movements of the right side are reduced.
- Vocal fremitus is increased in the right infraclavicular region.
- Percussion note is impaired.
- Breath sounds are bronchial.
- Coarse crepitations are present, not altered by coughing.
- Vocal resonance is increased. There is bronchophony.

Diagnosis: Fibrosis right upper lobe.

Case 5

A male aged 25 years, has cough, hemoptysis, loss of weight and fever for the past 1 year. Position of the trachea is shifted towards the left.

- Movements of the chest are reduced on the left supra and infraclavicular regions.
- Vocal fremitus is increased.
- Percussion note is impaired
- Breath sounds are cavernous over the left supraclavicular, suprascapular and infraclavicular regions
- Coarse crepitations are present, increasing with coughing (post-tussive crepitations)
- Vocal resonance is increased; whispering pectoriloquy is present

Diagnosis: Cavitation associated with fibrosis left upper lobe.

Physical examination of the chest helps to detect gross physical alteration of the lungs and other intrathoracic structures. For arriving at the etiological diagnosis, other clinical features help. For example, development of consolidation of the lung acutely, associated with fever and rusty sputum is suggestive of pneumonia, whereas a subacute or chronic consolidation may suggest tuberculosis or malignancy. Pulmonary collapse occurring in a heavy smoker should suggest malignancy whereas the same occurring after a road accident or seizure should suggest obstruction by a foreign body. Pleural effusion occurring acutely in a young adult with family history of tuberculosis may be due to the same cause, whereas a pleural effusion in a woman who had mastectomy for breast carcinoma three years earlier is most likely due to metastatic cancer.

Common Pathological Changes in the Lungs and Pleura (Table 12.7)

Consolidation

- Pneumonia (lobar)
- Tuberculosis
- Neoplasms—bronchogenic carcinoma, secondaries.
- Pulmonary infarction due to massive pulmonary embolism.

Cavitation

- Tuberculosis, usually in upper lobe.
- Lung abscess, usually in lower lobe.
- Bronchiectasis—lower lobes more commonly affected.
- Fungal infections—aspergillosis in post-tubercular cavity presenting as mycetoma
- Pleuropulmonary amebiasis.

Table 12.7: Physical signs elicitable over common pathological lesions

	Abnormality in shape of chest wall	*Movements of the chest*	*Mediastinal displacement (position of trachea and apex beat)*	*Vocal fremitus*	*Percussion note*	*Breath sounds*	*Vocal resonance Whispering pectoriloquy (WP)*	*Added sounds*
1. Pneumonic consolidation	Nil	Reduced	Nil	Increased	Dull	High pitched bronchial (tubular)	Increased, whispering pectoriloquy (present)	Fine Insp. creps in early stages, medium to coarse during resolution
2. Collapse	Flattening or retraction	Diminished or absent over the affected side	Towards the side of lesion	Usually diminished	Dull	Markedly decreased or absent. Bronchial, (a) if underlying bronchus is patent or (b) trachea is pulled to the same side or (c) there is associated consolidation	Absent or bronchophony and WP present	None. Crepitation if infected
3. Fibrosis	Retraction	Diminished	Towards the side of lesion	Diminished	Impaired or dull	Diminished or bronchial	Diminished or bronchophony	Coarse crepitations
4. Cavitation: Usually associated with fibrosis or consolidation	Retraction if associated with fibrosis, e.g. apical tuberculosis	Slightly decreased on affected side	None, or towards the side of lesion	Increased	Impaired	Bronchial, cavernous or amphoric when it is communicating with a bronchus	Increased WP present	Coarse creptitations. Post-tussive suction may be present If thin walled

Contd...

Contd..

	Abnormality in shape of chest wall	Movements of the chest	Mediastinal displacement (position of trachea and apex beat)	Vocal fremitus	Percussion note	Breath sounds	Vocal resonance Whispering pectoriloquy (WP)	Added sounds
5. Emphysema	Barrel shaped	Diminished	Nil	Decreased	Hyper-resonant. Liver dullness is shifted down, cardiac dullness is obliterated	Decreased in intensity, vesicular breathing with prolonged expiration	Decreased	Expiratory wheeze may be present. Crepitations if associated with bronchitis
6. Pleural effusion	Prominence of affected side	Reduced or absent on affected side	To the opposite side	Decreased	Stony dull	Diminished or absent, may be bronchial at the upper level of effusion	Decreased or absent, Rarely egophony at upper level	Pleural friction rub in some cases
7. Pneumothorax	Prominence	Reduced or absent	To the opposite side	Decreased or absent	Hyper-resonant	Diminished or absent. At times amphoric in open pneumothorax	Decreased or absent	Tinkling or metallic crepitation if fluid is present. Knocks may be present. Coin sound present
8. Hydropneumothorax	Prominence or bulge	Reduced or absent	To the opposite side	Decreased	Hyper-resonant above and stony dull below	Amphoric breathing in bronchopleural fistula	Decreased	Succussion splash. Coin sound present
9. Interstitial lung disease	Nil	Diminished	None	Usually normal	Normal	Harsh vesicular breathing with prolonged expiration	Normal or increased	Bilateral end inspiratory crepitation not influenced by coughing

- Cavitation of bronchogenic carcinoma (squamous)
- Congenital cysts
- Ruptured infected hydatid cyst.
- Vasculitis: Wegener's granulomatosis.
- Pulmonary infarct undergoing abscess formation.
- Pneumoconiotic nodules.

Collapse

Obstruction to bronchial lumen

- Tumors
- Bronchial carcinoma
- Bronchial adenoma (less common)
- Inhaled foreign body
- Bronchial casts/plugs (inspissated muscus/blood clots).

Pressure on the bronchus from outside

- Enlarged tracheobronchial lymph nodes in malignancy
- Lymphoma or primary tuberculosis
- Pressure of fluid in pleural effusion
- Pressure of air in tension pneumothorax.

Fibrosis

Replacement fibrosis—localized-variable extent

- Pulmonary tuberculosis
- Bronchiectasis
- All types of pulmonary suppuration
- Chronic pleural effusion.

Inhalation of irritants and dusts pneumoconioses, e.g. silicosis, asbestosis, fungal spores.

Interstitial lung diseases: Diffuse and uniform.

Pleural Effusion

Exudative fluid

It shows character of an exudate

- Tuberculosis
- Pneumonia—Syn: pneumonic and post-pneumonic effusions.
- Malignancy—primary in the lung or pleura and metastases from other sites.
- Pulmonary infarction.
- *Collagen disorders*: Systemic lupus erythematosus, rheumatoid disease.

Transudative fluid

It shows character of a transudate (hydrothorax).

- Congestive cardiac failure
- Nephrotic syndrome.
- Cirrhosis of liver
- Meig's syndrome—fibroma of the ovary, with pleural effusion.
- Sympathetic effusion in cases of subphrenic abscess, amebic liver abscess, acute pancreatitis.

Chylothorax

The pleural fluid is chylous (i.e.) milky due to globules of fat.

- Obstruction of thoracic duct caused by filariasis, malignancy
- Trauma to thoracic duct.

Hemothorax

Pleural fluid is hemorrhagic

- Malignancy
- Pulmonary infarction
- Trauma
- Less commonly, tuberculosis.

Empyema

Usually, it is the result of spread, of infection from a contiguous focus, e.g. bacterial pneumonias, lung abscess, or subdiaphragmatic abscess

- Esophageal perforation
- Thoracic surgery and thoracentesis
- Empyema may occur as part of generalized pyaemia.

Pneumothorax

- Spontaneous pneumothorax—rupture of subpleural bulla
- Trauma to lung due to rib fracture
- Secondary to underlying lung diseases such as tuberculous cavities, rupture of a cyst.

Lung Abscess

- Pulmonary infarction
- Rupture of pleural adhesions
- Bronchogenic carcinoma
- Perforation of esophagus
- Rupture of lung caused by faulty mechanical ventilation.

Hydropneumothorax

- Rupture of a tuberculous cavity, or other cavitating pulmonary lesions
- Trauma to the chest with rib fracture and injury to the lung
- Secondary infection in a pneuothorax
- Postoperative—following surgery in the thorax or upper abdominal organs
- Infection by gas producing organisms.

CHAPTER

13 Investigations in Respiratory Diseases

C Sudheendra Ghosh

Examination of sputum, Radiology of the chest, Computed tomography, Magnetic resonance imaging, FDG-PET, Bronchoscopy, Lung biopsy, Investigations in pleural diseases, Thoracoscopy and pulmonary function tests

EXAMINATION OF SPUTUM

Examination of sputum gives invaluable information in respiratory diseases. This is mandatory in all cases where infections or neoplasia are suspected.

Collection of Sputum

A clean widemouthed bottle should be used for sputum collection. Most patients find it easier to bring out sputum early in the morning soon after waking up. Sputum brought out from the lower respiratory tract should be collected without contamination by saliva. When sputum is scanty or thick and sticky, proper hydration of the patient and administration of expectorants such as ammonium chloride or bromhexine make expectoration easier. In those with inability to cough, suitable physiotherapy such as adoption of appropriate postures and assistance to coughing helps to clear the air passages.

When sputum cannot be obtained by these simple methods, more invasive procedures such as bronchoscopic aspiration, bronchoscopic lavage and transtracheal aspiration may become necessary. To assess the total daily output of sputum it should be collected for 24 hours.

Inspection

Note the color, smell and quantity. The sputum is viscid and yellow in acute bronchitis, bronchiectasis and lung abscess. It is white and mucoid in chronic bronchitis, bronchial asthma and pulmonary tuberculosis. Rusty sputum is suggestive of pneumonia. Presence of Curshman's spirals which are bronchial casts suggests bronchial asthma and allergic bronchopulmonary aspergillosis. Watery and blood stained sputum suggests pulmonary edema. Causes of hemoptysis are described in chapter 12. Chocolate-colored sputum may suggest amebiasis. Serial reduction in the quantity of sputum and change in its physical characteristics are bedside parameters to monitor improvement in the condition. Intense foul smell should suggest chronic suppuration as in bronchiectasis and lung abscess.

Three Layer Test

Allow the sputum to stand in a conical glass. In conditions such as bronchiectasis and lung abscess, it may form three distinct layers—thick nummular purulent sputum below, serous fluid in the middle and froth above.

Microscopy

Usually sputum is examined microscopically after staining. Unstained fresh specimen can be examined as a wet-preparation to reveal *Entamoeba histolytica*, and ova of *Paragonimus* if these infections are suspected. If the sputum is negative it can be concentrated by centrifugation and this gives higher positivity rates. Wet staining with aqueous methylene blue helps to detect malignant cells.

A proper specimen of sputum should reveal alveolar macrophages. Gram stain, Ziehl-Neelsen's stain, fluorescent microscopy and Papanicolaou stain are done according to the indication.

Gram's Staining

Make a thin smear from the mucoid or purulent part of the sputum. Fix it by drying over a flame. Pour methyl violet so as to cover the entire slide and allow to remain for one minute. After pouring off the excess stain, the smear is treated with Gram's iodine solution for 1 minute and decolorized with alcohol for 1 minute. The smear is washed with water. Counterstaining is done with dilute basic fuchsin for half minute. The smear is dried and examined with oil immersion objective. Gram's staining reveals bacterial pathogens.

Staining for Leukocytes

The presence and distribution of leukocytes in the sputum will also give clues to diagnosis. In pyogenic infections almost all the leukocytes may be neutrophils. In asthma, the proportion of eosinophils is increased. The predominance of neutrophils or eosinophils in the sputum of asthmatic patients is of some help in indicating whether infections or allergic factors are responsible for exacerbations.

Ziehl-Neelsen Staining

This is done to detect mycobacteria, particularly tubercle bacilli in sputum. Fix the smear by passing over a flame. Cover the whole slide with concentrated carbol fuchsin. The slide is heated for 5 to 7 minutes so that fumes appear but not to boil. Excess stain is poured off and the smear is decolorized using 20% sulfuric acid and washed with water repeatedly till the washings are colorless. Counter-staining is done with 1% aqueous methylene blue for 30 seconds. The smear is dried and examined under oil immersion. Tubercle bacilli will be seen as small red rods. A minimum of two bacilli should be seen to call the smear acid fast bacilli (AFB) positive and at least 100 oil immersion fields should be examined.

Detection of tubercle bacilli is conclusive evidence for the diagnosis of pulmonary tuberculosis. There should at least be 50 thousand tubercle bacilli per mL of sputum, if it has to be smear positive. Even in genuine pulmonary tuberculosis, sputum may be negative if the bacterial population is smaller, the lesion does not communicate with air passages or if the patient has received partial or complete treatment. Table 13.1 shows grading of AFB smears.

Table 13.1: Grading of AFB smears (Taken from Revised National TB Control Programme, India)

Examination	*Result*	*Grading*	*No of fields to be examined*
More than 10 AFB per oil immersion field	Positive	3+	20
1–10 AFB per oil immersion field	Positive	2+	50
10–99 AFB per 100 oil immersion fields	Positive	1+	100
1-9 AFB per 100 oil immersion fields	Scanty	Record exact seen number	200
No AFB per 100 oil immersion fields	Negative	-	100

Papanicolaou Stain

It is done to study the cytological abnormalities in sputum, detect and identify malignant cells and demonstrate the nature of bronchial casts.

Fluorescent Mircoscopy

It is useful when large number of sputum specimens have to be examined for tubercle bacilli. It is much more sensitive than acid fast staining, but it requires special staining methods and fluorescent microscope. The equipment is costly and it demands special skill for proper use. Though, it is more expensive it is useful when Ziehl-Neelsen staining is negative.

Microbiological Examination

This consists of culture of the sputum and tests for drug sensitivity. For reliable results the sputum should be free from contamination by organisms from the mouth and upper respiratory tract.

Newer rapid methods to do AFB cultures and drug sensitivity studies are now available, e.g. BACTEC-radiometric method and lucifer myco-bacteriophage fluorescence-technique.

RADIOLOGY OF THE CHEST

A standard posteroanterior view radiograph known commonly as chest X-ray PA view is a basic investigation in chest diseases and it reveals morphological changes in thoracic structures. For P A view the film is kept in apposition with the chest wall in front while the source of X-ray is kept behind. PA view is used to study the heart and lungs and other soft tissues. In the majority of cases, PA view is sufficient to give the diagnosis and this is the investigation of choice.

When lobar or segmental localization of pulmonary lesions is desired, a *lateral view* is also necessary. The lateral view also brings out the relationship of the pulmonary lesion to mediastinal structures. The anterior and posterior pleural recesses are revealed clearly in the lateral view. Interpretation of a lateral view is sometimes difficult because of the superimposition of both lungs.

Right and left *anterior oblique views* are taken to study abnormalities of the heart such as atrial and ventricular enlargement and others.

The quality of a chest radiograph is considered satisfactory if the lateral borders of the vertebra are seen through the cardiac shadow, but not the intervertebral space. If intervertebral spaces are also very clearly seen, it suggests overexposure of the film. If the vertebral bodies themselves are not seen, the film is underexposed. In a properly positioned P A view, the vertebral spines run midway between the medial ends of the clavicles.

Positioning of Patient for X-rays

PA view is used for studying the lungs and mediastinum. Anteroposterior view (AP view) (i.e.) the source of X-rays is in front and the film behind-is usually taken to study the vertebral column and bony thorax. When a clear view of the upper zones is desired without overlap by the clavicles, PA view is taken with the patient in hyperextended lordotic position—Lordotic view. Lateral view is taken to bring out details of vertebral and intervertebral disks.

Contrast Studies

The esophagus is visualized by a barium swallow examination. Barium swallow picture taken with the patient in the right anterior oblique position reveals enlargement of the left atrium. Esophagus may show indentation by the aortic arch or abnormal arteries such as aberrant subclavian.

Bronchogram is done to delineate the bronchial tree. Pictures are taken after instilling iodinated contrast medium into the bronchial tree and adjusting the position of the patient for the dye to gravitate. The main indication for bronchogram is to confirm the presence and extent of bronchiectasis and to demonstrate intrabronchial obstruction.

Figures 13.1 to 13.14 give classic radiological pictures of some of the respiratory diseases. Even today chest radiography remains the prime investigation to detect morphological abnormalities in the chest.

Fluoroscopy

Observing the action of the heart and lungs on the fluorescent screen is fluoroscopy. Movements of the heart and great vessels, respiratory changes in the translucency of the lungs and movement of the diaphragm can be observed. Modern machines use TV screens for better visualization and avoidance of exposure to the examiner.

Systematic Examination of Chest Radiograph

Look for abnormalities over the soft tissues. In surgical emphysema, air is seen between tissue spaces. The ribs should be traced from behind forwards. Abnormalities such as supernumerary ribs, cervical ribs, absence of ribs, abnormal ribs, fractures and erosions should be identified.

Next inspect the diaphragm. Normal level of diaphragm on right side is 5th or 6th intercostal space in the midclavicular line. Level of diaphragm is usually lower on the left than that on the right side by 2 to 3 cm. Cardiophrenic and costophrenic angles are clearly visualized. The diaphragm is elevated in conditions such as pulmonary collapse and fibrosis, increased intra-abdominal pressure, hepatosplenomegaly, subdiaphragmatic abscess and diaphragmatic paralysis.

Features of normal skiagrams of the chest:

1. Trachea is central
2. Both lung fields are symmetrically translucent
3. The cardiophrenic angles and costophrenic angles are clearly seen
4. Cardiothoracic ratio is less than 50%.

Cardiothoracic Ratio

The transverse diameter of the heart should be less than 50% of the width of the bony thorax. In cardiomegaly, this ratio is higher.

For purposes of description, lung fields are divided into upper, middle and lower zones by two horizontal lines drawn along the lower margins of the anterior ends of the second and fourth ribs.

Some Common Radiographic Abnormalities

Opacities

Sharp localized opacities may be caused by radio-opaque foreign bodies in the tracheobronchial tree, lungs or esophagus.

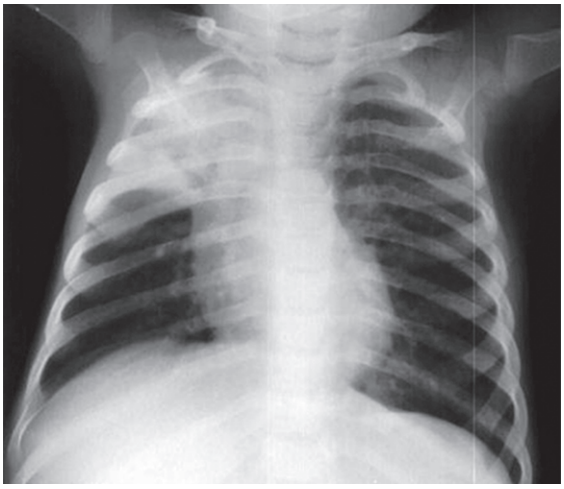


Fig. 13.1: Consolidation right upper zone. *Note:* Uniform opacity with clearcut lower margins. No displacement of the mediastinum and trachea. Note also the air filled trachea and bronchus (air bronchogram) common cause pneumonia

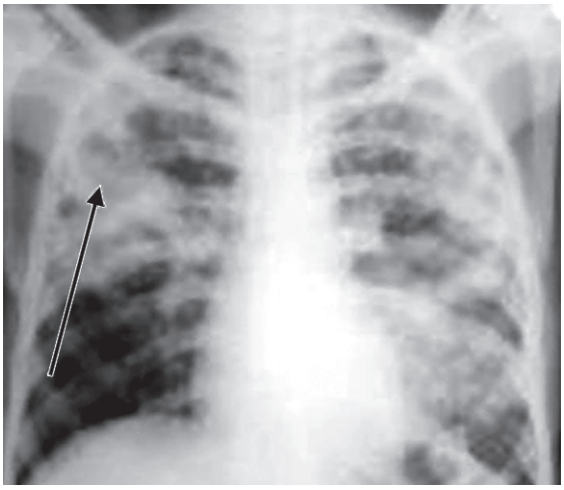


Fig. 13.3: Fibrocavitary tuberculosis. *Note:* Bilateral diffuse and circumscribed opacities more in the upper zones with cavitation (central clearing-arrow)

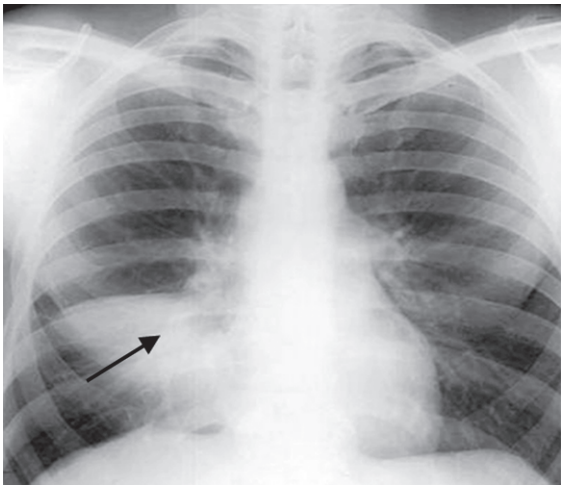


Fig. 13.2: Middle lobe consolidation right. *Note:* Uniform haziness right midzone with clearcut margins. Common cause tuberculosis or pneumonia arrow points to air bronchogram

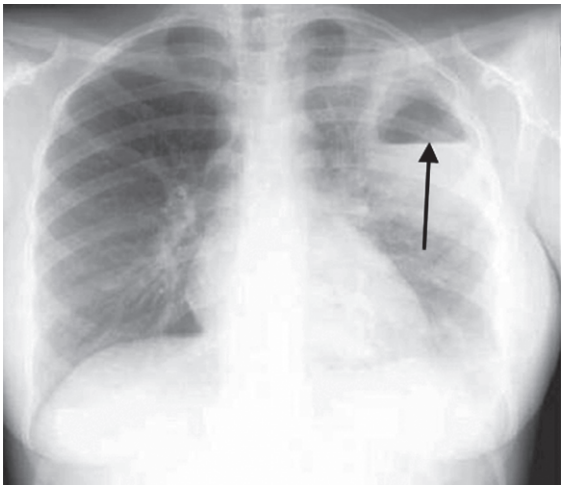


Fig. 13.4: Lung abscess left upper zone. *Note:* The cavitary parenchymal lesion with horizontal air fluid level (arrow). Cavity is thick walled. Part of the pus has been coughed out

Diffuse Opacities

These opacities may vary in size, further details are given in (Table 13.2).

Location of Lesions

Primary tuberculosis may affect any part of the lung, but postprimary tuberculosis affects the upper zones more often. Abscesses and bronchiectasis are more common in the lower zones. Bronchogenic carcinoma is seen adjacent to the mediastinum or peripherally. Other types of neoplasms may arise peripherally. Pancoast tumor is seen at the apical region. Malignant secondaries are seen more towards the lower zones.

Table 13.2: Features of diffuse opacities in the chest X-ray

Diffuse lesions >1 cm in diameter	*Diffuse lesions < 1 cm in diameter*	*Pin head sized lesions*
Bronchopneumonia	Bronchopneumonia	Interstitial lung diseases such as fibrosing alveolitis
Pulmonary secondaries	Miliary tuberculosis	Sarcoidosis
Bronchopneumonic form of tuberculosis	Tropical eosinophilia	Alveolar microlithiasis
hemosiderosis,	Pneumoconiosis	
Pulmonary mycoses		Miliary tuberculosis

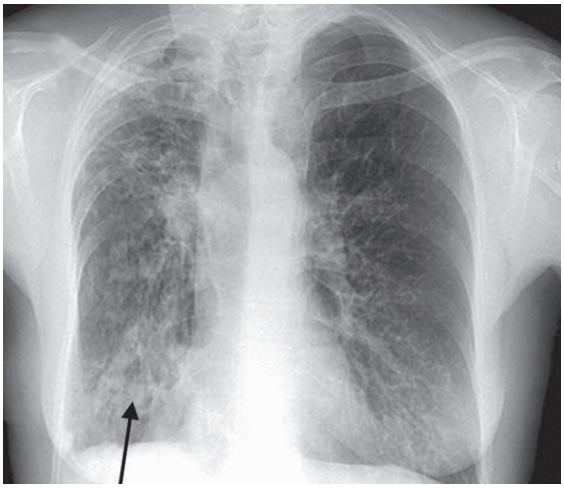


Fig. 13.5: Bilateral bronchiectasis more affected on the right lower zone. Note the dialated ectatic bronchi which are filled with exudates. Confirmation of the diagnosis is by bronchography or by CT

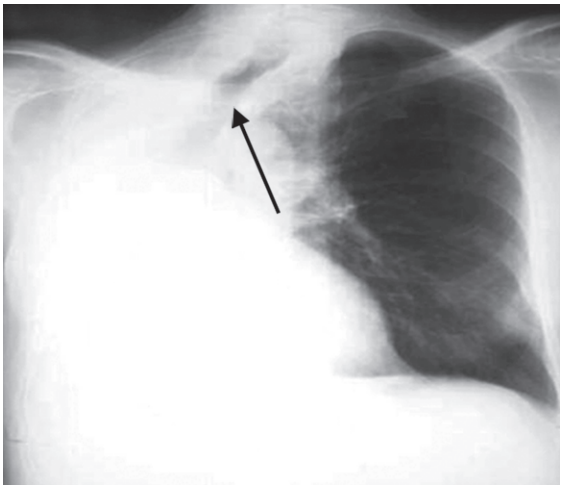


Fig. 13.7: Collapse right lung. Note the uniform opacity caused by collapsed lung. Trachea (arrow) and mediastinum are displaced to the right (arrow)

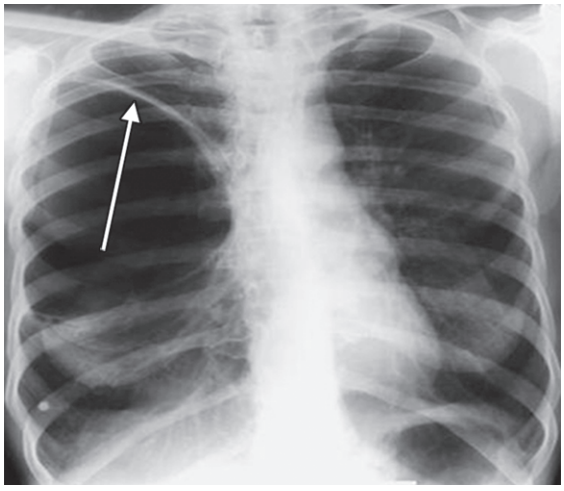


Fig. 13.6: Emphysema. Note hypertranslucency of the lungs, enlarged lung volume, depressed diaphragm, and the inflated appearance of the lungs. Arrow points to an emphysematous bulla with thin walls

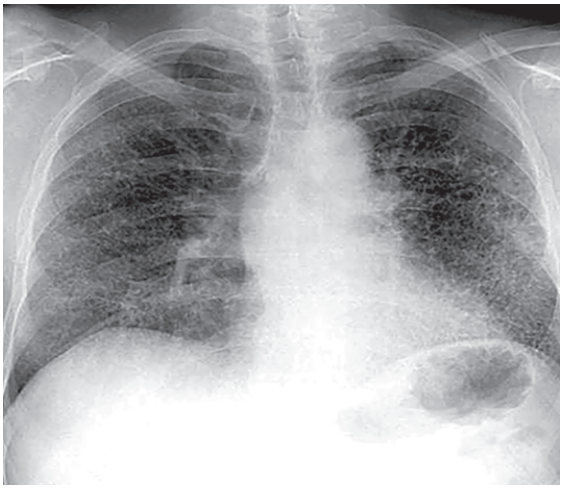


Fig. 13.8: Interstitial lung disease. Reticular shadows indicating diffuse inter- and intralobular septal thickening. See also CT scan

Pulmonary Consolidation

Lobar consolidation appears as an opacity conforming to the lobar anatomy. The shadow is homogenous with clearcut margins. There are no compensating changes such as shift of trachea or mediastinum. The larger bronchi containing air can be seen through the consolidation as translucencies—air bronchogram (Figs 13.1 and 13.2). Exact identification of the affected lobe and segment can be done by taking the P A and lateral views.

Pulmonary Collapse

This gives rise to homogenous opacity with clear-cut margins, often concave due to reduction in pulmonary volume. When collapse is massive there is shift of adjacent structures such as trachea, mediastinum or diaphragm towards the lesion (Fig. 13.7).

Pulmonary Fibrosis

This produces a nonhomogenous opacity often with irregular margins. There is pull on the adjacent structures towards the lesion.

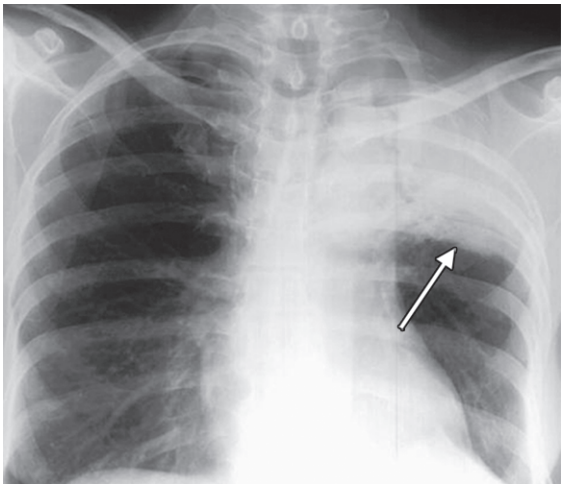


Fig. 13.9: Bronchogenic carcinoma. Left upper/zone consolidation due to tumor and collapse. Rib erosion (arrow) suggests malignant lesion—bronchogenic carcinoma



Fig. 13.11: Pulmonary metastases. Bilateral cannon ball shadows—common primaries thyroid, bone and viscera

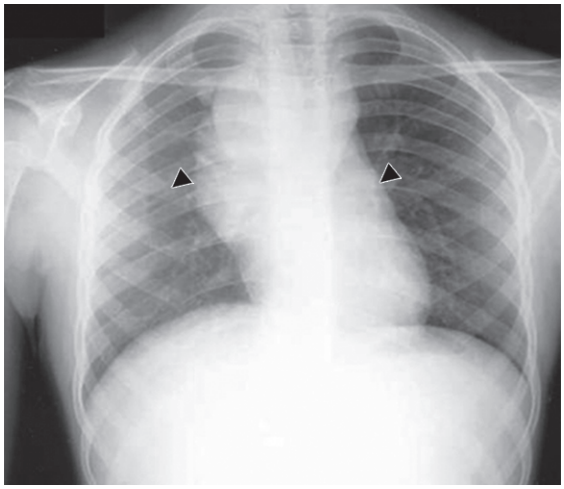


Fig. 13.10: Lymphoma. *Note:* The bilateral paratracheal lymphadenopathy (arrowheads) is a common cause of mediastinal syndrome

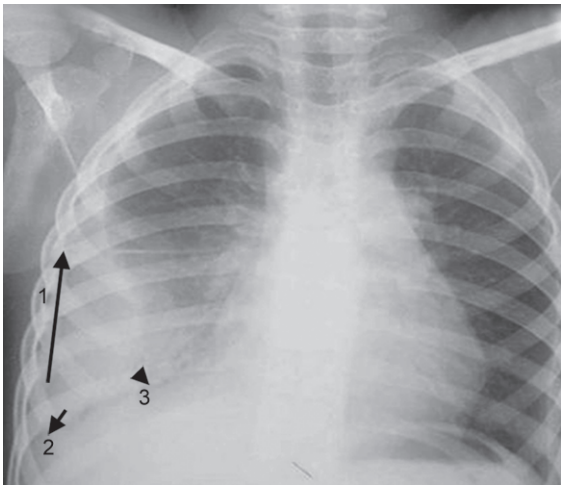


Fig. 13.12: Pleural effusion right. *Note:* Hazy opacity occupying the right lower part, rising in the axilla (long arrow 1). The costophrenic (short arrow 2) and cardiophrenic angle (arrowhead 3) are obliterated in massive effusions, mediastinum is displaced to the opposite side

Cavities, bullae and cysts: Ring shadows with thin walls are called cavities. There may or may not be fibrosis. The most common cause for cavities with surrounding fibrosis is pulmonary tuberculosis (Fig. 13.3).

Presence of fluid level in a cavity suggests lung abscess. Abscess commonly results from breaking down of pneumonia. Necrosis of the center of a malignant lesion may also resemble abscess cavity (Fig. 13.4).

Thin-walled cavities are seen in emphysematous bullae and congenital cysts. Bullae and cysts are clear without pulmonary markings within them. Unlike pneumothorax, they do not cause shift of the mediastinum (Fig. 13.6).

Coin Shadows

A single regular or irregular circular opacity of the size of a coin is a diagnostic problem. It can be due to inflammatory lesions or benign or malignant

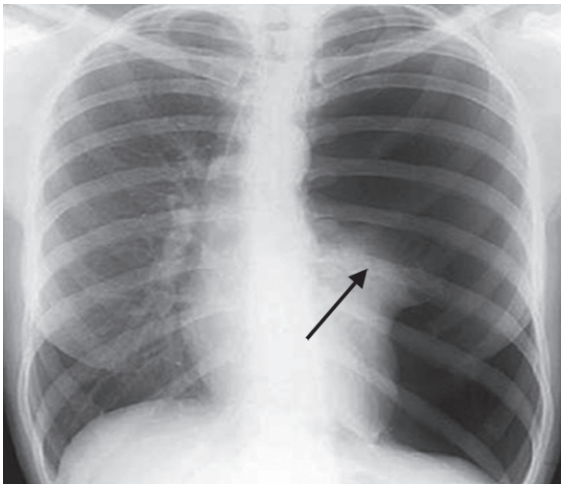


Fig. 13.13: Pneumothrax left. *Note:* 1. The increased translucency and absence of normal bronchovascular markings 2. Trachea and mediastinum shifted to opposite sides. 3. Collapsed lung margin (arrow) seen close to the hilum

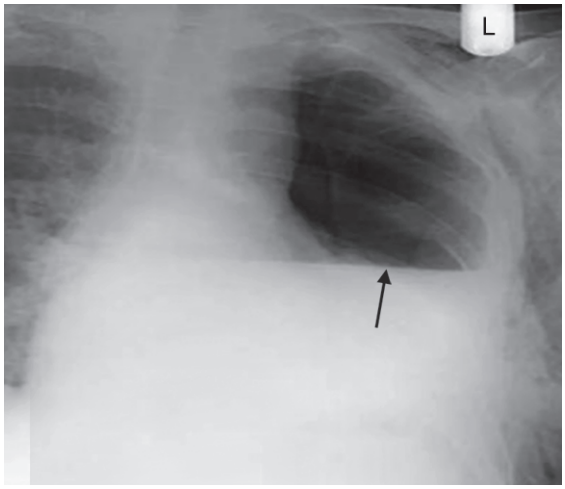


Fig. 13.14: Hydropneumothrax left. Note horizontal air fluid level indicating air above and fluid below with the margin in between (arrow). This fluid level will shift with the position of the patient

neoplasms. Many a time detection of such lesions may end up with pulmonary resection, especially when their nature is in doubt. Smooth rounded shadows with no evidence of regional lymphadenopathy might suggest benign nature. Spicules running into the lung fields from the irregular border may suggest malignancy. If the coin shadow is seen to grow rapidly (within weeks) it often suggests an inflammatory mass. Growth of malignant lesion is slower. Investigations like sputum cytology, bronchoscopy, examination of bronchoalveolar lavage fluid, bronchoscopic brush biopsy or transbronchial biopsy may help in diagnosis. Biopsy of accessible lymph nodes, CT aided fine needle aspiration biopsy and thoracotomy with open biopsy of the pulmonary lesion may be required when the nature of the lesion is in doubt.

Radiological Clues to Suspect Malignancy

1. Mass lesion or coin shadow
2. Mediastinal widening due to enlargement of lymph nodes (Fig. 13.10)
3. Rib erosion and rib fracture (Fig. 13.9)
4. Phrenic nerve paralysis in the presence of mediastinal mass
5. Presence of pleural effusion (Fig. 13.12)
6. Cannon ball shadows (Fig. 13.11).

Translucencies

Normal lungs are translucent, but the bronchovascular markings can be seen as branching opacities throughout the lung tissue.

Hypertranslucency may be due to over distention of the lung as in emphysema, or collection of air within cysts or bullae or in the pleural cavity.

Emphysema: The lung volume increases leading to over distention of the bony thorax. The ribs rise more horizontally and rib spaces are widened (Fig. 13.6).

The diaphragm is flat and is pushed down. In the fluorescent screen, the diaphragmatic excursions are seen to be less. Even during full expiration the lungs are hypertranslucent. When emphysema is bilateral, there is no shift of midline structures. Localized emphysema may be seen in compensatory emphysema and in partial obstruction to bronchi.

Collection of Free Air

This is seen in bullae, cysts, and in pneumothorax. This is distinguished from emphysema by the absence of lung markings (Figs 13.6 and 13.13).

Pleural Lesions

Pleural effusion appears as a uniform opacity filling the costophrenic angle and at times the cardiophrenic

angle also, with a higher level towards the periphery and lower level medially. When the fluid is massive, the mediastinum and trachea are shifted to the opposite side. When the fluid is small in amount, a lateral view is more helpful to demonstrate fluid more clearly in the posterior diaphragmatic recess. Even when the pleural fluid collection is only 100 mL, the lateral view reveals it, whereas larger amount (200 mL, or more) are only clearly visible as blunting of the costophrenic angles in the PA view (Fig. 13.12).

Lateral Decubitus Position

This view helps to distinguish the presence of fluid in pleural cavities from fluid in cavities in the lungs and to differentiate a solid mass from free pleural fluid. The patient lies on the affected side for 15 minutes by which time free fluid in the pleural cavity gravitates to the dependent part. PA film taken in this position reveals that the fluid has tracked to the dependent part. Loculated fluid and solid masses do not show this change.

Pneumothorax

The affected side is hypertranslucent with widening of the ribs, and shift of midline structures to opposite side. The lung is collapsed to varying degrees and its free margin can be seen distinctly (Fig. 13.13).

Hydropneumothorax

In addition to findings of pneumothorax, the fluid shows homogenous shadow occupying the lower part, with a horizontal upper margin, which shifts with change of position of the patient (Fig. 13.14).

Tomography

This is the procedure in which radiographs are taken in different planes. This brings into view the extent and location of lesions and greater details of the central parts. With the free availabity of CT this investigation is seldom done at present.

COMPUTED TOMOGRAPHY

CT has become the most useful imaging technique in the evaluation of chest diseases, next to plain radiograph. Tomographic pictures help to produce better diagnostic images.

Essentially three modes of CT imaging are in vogue which give specific advantages:

1. CT scan-conventional: Sections at 10 mm interval are produced while the patients remain stationary.
2. High resolution CT (HRCT): In this the sections are made at 2 mm thickness.
3. Volumetric spiral/helical CT.

Spiral CT is a recently introduced advancement in technology. In spiral CT, large volume of the thorax can be imaged in a single breath hold. In conventional CT, repeated breath holdings are needed. If the patient does not breathe to the same extent for all pictures, for each section misregistration of sequential events may lead to non-recognition of small lesions.

Indications for Chest CT

CT is used as a second line diagnostic study for problems that are unresolved by plain X-ray films.

1. Mediastinal or hilar contour abnormality: This raises the possibility of vascular pathology such as vascular dissection, aneurysm, congenital anomaly, normal variant or distortion or by tumor.
2. Pulmonary parenchymal nodule, mass or infiltrate.
3. Diffuse abnormality on plain film if suggestive of parenchymal or small airway pathology, HRCT is indicated.
4. Combined cases of complex, pleural and parenchymal pathology. Here contrast enhanced study is indicated.
5. Chest wall and spine pathology: Because of the curvature of chest, single plain film projection is not adequate for full evaluation. Transaxial format of CT enables better analysis of the location and extent of such lesions.
6. Pathology involving cervico thoracic or thoracolumbar junctional regions.
7. Screening of patients whose chest X-ray is negative but clinical condition suggests occult intrathoracic pathology. For example:
 a. Metastatic nodule in patients with extrathoracic malignancy.
 b. Patients with myasthenia gravis to rule out thymoma.
 c. Patients present with intermittent hemoptysis but with negative clinical findings or sputum findings, persistent wheezing, suspected of having carcinoma or bronchiectasis.

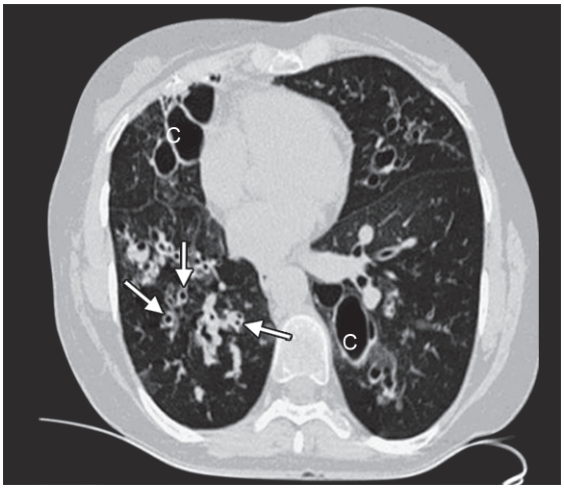


Fig. 13.15: CT showing bilateral bronchiectasis. *Note:* Dilated cystic bronchi on both sides (arrows)

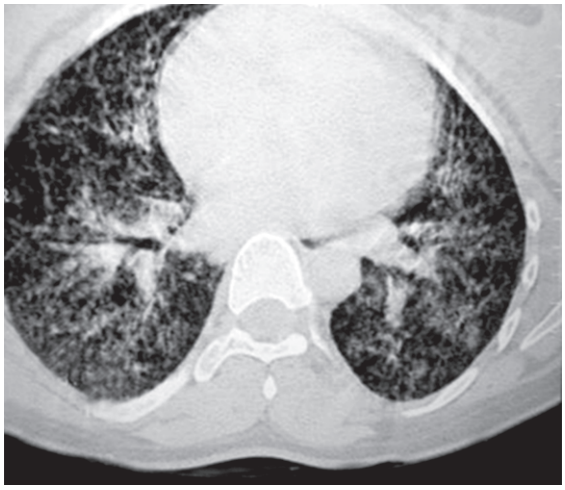


Fig. 13.17: CT showing extrinsic allergic alveolitis. *Note:* Reticulonodular shadows distributed bilaterally

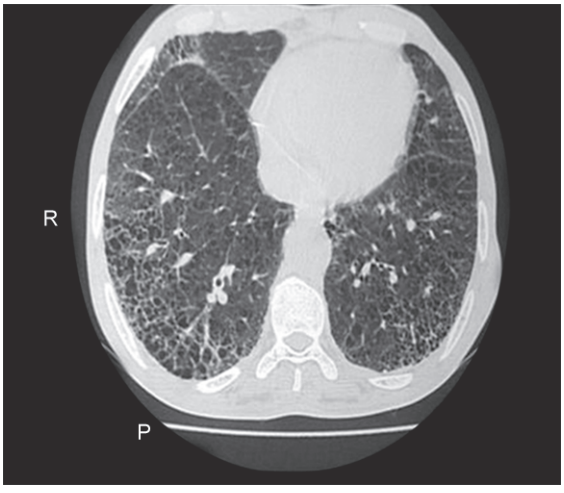


Fig. 13.16: CT showing honey-comb lung in interstial pulmonary fibrosis (IPF). *Note:* The multiple lesions, more abundant in the lower zones

d. Evaluation of pulmonary parenchyma in patients with abnormal pulmonary function tests and normal X- ray chest.
e. Suspected pulmonary embolism.

8. Evaluation of patients with occult source of infection especially in immunocompromised patients (Figs 13.15 to 13.17).

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) is required for selected patients with diseases of the heart, lungs and the mediastinum. MRI is also very helpful in the assessment of lesions such as direct invasion of the chest wall, mediastinum and diaphragm by lung cancer or malignant mesothelioma.

FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY (FDG-PET)

FDG-PET is a nuclear medicine technique that labels the glycolytic pathway of tumor cells or other metabolically active cells to identify glucose-avid tissues. This has better sensitivity and specificity for detecting lymph node metastases. This can help to direct the surgeon toward particular lymph node groups that show increased activity on PET scanning. PET scan when combined with CT scan (PET-CT) can yield better anatomical resolution and disease activity status.

BRONCHOSCOPY

It is the procedure by which the interior of the tracheobronchial tree is inspected using a bronchoscope. Both rigid and flexible bronchoscopes are available.

Through the rigid bronchoscope instruments like cutting forceps, biopsy forceps and suction tubes can be introduced. Rigid bronchoscope has its limitations. It has to be introduced under general anesthesia. It can reach only upto the openings of the segmental bronchi. The upper lobes cannot be satisfactorily visualised. But it has certain advantages

for removing foreign bodies. It also provides a better airway, especially during bronchoscopy in patients with hemoptysis.

The flexible fibreoptic bronchoscope is more popular. It can be introduced under local anesthesia as a bed side procedure and can reach upto peripheral airways. It can visualize the upper lobe and its segments. Transbronchial biopsies and bronchoalveolar lavage from specific areas can be done with this instrument. A side attachment permits a second person also to watch the bronchoscopy.

Indications for Bronchoscopy

1. Mass lesions, unresolved pneumonias, suspected malignancy
2. Hemoptysis—both as an emergency or elective procedure
3. Diagnosis of endobronchial lesions, strictures and atelectasis
4. To obtain specimens by bronchial brushing, bronchoalveolar lavage and biopsies.

Bronchoalveolar Lavage (BAL)

This procedure is done to obtain washings from a particular region of the bronchial tree. It is of diagnostic value in infective conditions, neoplasms, pulmonary alveolar proteinosis and sarcoidosis. It is particularly useful to get cytological specimen from peripheral neoplasms. Around 5 to 10 ml of normal saline is instilled into the segmental or lobar bronchus through the suction line of fiberoptic bronchoscope and immediately aspirated back. The specimen is collected in a suitable receptacle for biochemical, cytological and microbiological studies.

Endobronchial Ultrasound Guided Needle Aspiration (EBUS-NA) and Endoscopic Ultrasound Guided Needle Aspiration (EUS-NA) use bronchoscope/endoscope with an ultrasound probe at the end and a working channel through which a catheter with a needle can be passed. Both tests allow direct visualization of the lesion being sampled. The *CT fluoroscopy* and *virtual bronchoscopy* are other investigations undertaken at times.

LUNG BIOPSY

This is done to establish the diagnosis in localized or generalized lesions when other noninvasive techniques fail. Biopsy is also necessary to institute appropriate anticancer therapy which relies a great deal on the histological picture.

Lung biopsy can be done through a bronchoscope or percutaneously.

Transbronchial Lung Biopsy

Through the bronchoscope, the biopsy forceps is introduced and a piece of tissue is biopsied.

Percutaneous Needle Biopsy

Several instruments are available. Fine needle aspiration biopsy is done using a thin long needle. It is helpful in the diagnosis of lesions situated close to the chest wall beyond reach of the bronchoscope. The site for biopsy can be determined from PA and lateral view skiagrams.

Transthoracic needle aspiration can be done using needles of 18 to 24 gauge size passed through the chest wall under ultrasonographic, fluroscopic or CT guidance, after anesthetising the part. The aspirate is subjected to cytological examination and microbiological tests to identify bacterial and fungal organisms. Transthoracic needle aspiration is of great value in the diagnosis of solitary pulmonary nodules and other peripherally-situated lesions.

Other instruments used for lung biopsy include the screw needle, cutting needles *(Trucut and Vim Silvermann's)* and trephines. With simple, unaided biopsy procedure, the success rate is around only 10%. Complications include hemorrhage and pneumothorax.

INVESTIGATIONS IN PLEURAL DISEASES

In addition to radiography, other main investigations include study of the pleural fluid, pleural biopsy, diagnostic artificial pneumothorax and CT scan. In pleural effusion due to respiratory diseases, pleural aspiration should be done without fail. In pleural effusion occurring as part of generalized edema, pleural aspiration is often avoided, if the fluid clears when the edema is treated.

Indications for Pleural Aspiration

Therapeutic

a. As an emergency life-saving procedure: When a massive pleural effusion or bilateral pleural

effusions lead to respiratory distress or ventilatory insufficiency, emergency aspiration is to be done. Sufficient fluid as may be required to give relief is aspirated, When there is bilateral effusion, the side with greater amount of fluid is preferred.

b. As an elective procedure: The pleural fluid is removed by repeated aspiration at suitable intervals so as to clear the pleura as early as possible and avoid complications like collapse of the lung and pleural fibrosis.

Diagnostic Indications

The pleural fluid is aspirated for diagnostic investigations.

Procedure for Pleural Aspiration

Patient should be made to sit in the bed or on a stool leaning forward with both arms and head supported on a cardiac table kept in front. If available, the chest X-ray should be verified to confirm the site and side of effusion. The site of maximum dullness to percussion should be selected for aspiration. This generally coincides with the lowest part of fluid collection. The part is anesthetised by local infiltration with 2% lignocaine, using a 5 ml disposable syringe and 5 cm long needle. Local anesthetic should be infiltrated layer by layer upto the pleura. Withdrawal of pleural fluid by gentle suction would confirm that the pleural cavity is reached. 10 to 15 mL of fluid can be withdrawn for the preliminary tests and the needle removed. Sterile towels are used to drape the area. A standard pleural aspiration needle with attached flexible rubber tube and a three-way tap is used for fluid withdrawal. The aspiration needle with the three-way tap kept closed is gently, but firmly, introduced into the pleural space through the anesthetized area. Entry of the needle tip into the pleural space will be felt as a sudden release of resistance. Pleural fluid is aspirated using a 20 ml syringe with suitable manipulation of the three-way tap and collected in a container. Care should be taken to avoid entry of air into the pleural cavity during inspiration. 1000-1500 ml of pleural fluid can be aspirated at one sitting if the patient remains comfortable. Over zealous aspiration of larger quantities may precipitate pleural shock later.

Indication for Stopping Aspiration

1. Generalized chest pain or feeling of tightness in the chest develops
2. Patient gets intractable cough with expectoration of thin frothy blood stained sputum
3. The fluid becomes progressively blood stained and
4. Signs of shock—faintness, sweating and hypotension develop.

Repeated manual withdrawal with a syringe can be avoided by using a Potain's jar which can be connected to the needle, and fluid aspirated by creating negative pressure in the jar. If the pleural fluid is purulent it should be completely aspirated in one or more sittings. If the fluid is purulent and thick, drainage is done through a wide rubber tube introduced in the intercostal space surgically—*intercostal drainage.*

Complications of Pleural Aspiration

1. *Pleural shock:* If the pleura is not properly anesthetized the patient may develop hypotension and shock on puncturing the pleura. If this happens aspiration should be stopped and pressor agents such as dopamine or dobutamine in a dose of 200 mg added to 500 mL 5% glucose is given as an IV drip and the drip is adjusted based on BP reading. Around 7 to 10 mcg/kg/mt is required in most cases. Adrenaline 1 mL of 1/1000 solution given SC is very effective in most cases. Hydrocortisone 100 to 300 mg IV or betamethasone 4 to 12 mg IV help to tide over the crisis. If allergy to local anesthetic is suspected, an antihistaminic like chlorphen-eramine maleate in a dose of 25 to 30 mg may be given. IM Other supportive measures include the administration of oxygen, hot tea, and sedation. Diazepam 5 mg given IV or 10 mg given orally helps to allay anxiety and produce sedation.
2. *Hemorrhage into pleura:* If the pleural aspirate becomes progressively blood stained, aspiration should be stopped.
3. *Pulmonary edema:* When the lung which was remaining collapsed for a long time suddenly expands, it may lead to pulmonary edema. This gives rise to cough with expectoration of frothy blood-stained sputum. If this happens aspiration should be stopped. At subsequent sittings only smaller quantities should be withdrawn.

4. *Injury to lung* by the aspirating needle gives rise to hemothorax, pneumothorax or hemoptysis. This should be avoided by suitable positioning of the needle tip and gentle withdrawal of the needle as the pleural space is emptied.
5. *Accidental entry of air into the pleura* converts pleural effusion into hydropneumothorax. This should be avoided by taking proper care during aspiration. In most of the cases the air gets absorbed even without special measures.
6. *Infection of the pleura:* This leads to the development of pyothorax. This should be prevented by following strict asepsis.

Examination of Pleural Fluid

Gross Appearance

The pleural fluid may be clear and watery, straw colored, turbid, hemorrhagic, milky or purulent. It may be a transudate or exudate (Table 13.3).

Common causes of transudate effusion: All cause of gross generalized edema such as congestive heart failure, nephrotic syndrome, hypoproteinemia and cirrhosis of liver may be accompanied by passive pleural effusion, which clears up along with the generalized edema on treatment.

Table 13.3: Differences between transudates and exudates

Characteristics	*Transudate*	*Exudates*
Specific gravity	Below 1010	Above 1010
Appearance	Clear and thin	Thick and opalascent or opaque
Protein content	Below 3g/dL	Above 3g /dL
Microscopy	Only a few cells	Increase in leukocytes and presence of malignant cells. Lymphocytes increase in tuberculosis. Neutrophils are increased in pyogenic infections. Eosinophils are increased in tropical eosinophilia, allergic disorders, helminthiasis and fungal infections
Microbiology	Fluid is sterile	Presence of organisms can be detected in infective conditions
Pleural fluid/ serum proteins ratio	< 0.5	>0.5
Pleural fluid /serum	< 0.6	> 0.6
LDH ratio		
LDH concentration	Less than 2/3 of upper limit of normal serum LDH	More than 2/3 of upper limit of normal serum LDH

Common causes of exudate effusion: All forms of pleurisy—tuberculosis, pyogenic infections, viral infections, dyscollagenoses, malignant lesions.

Causes of hemorrhagic pleural fluid: Malignancy, pulmonary infarction, traumatic lesions, hemorrhagic diseases, occasionally tuberculous pleural effusions.

Chylous Fluid

True chylous fluid is caused by the presence of fat globules and it clears on adding fat solvents like ether. This occurs in lymphatic obstruction caused by malignant secondaries and filariasis. Pseudochylous appearance is due to the presence of disintegrated leukocytes. This does not clear on adding ether. Common biochemical tests done on the pleural fluid are the estimation of proteins, LDH, adenosine deaminase and interferon gamma. Adenosine deaminase (ADA) and interferon gamma levels in pleural fluid may help to determine the etiology. ADA levels > 70 units/L and/or interferon gamma levels > 200 pg/mL are virtually diagnostic of tuberculous infections. These may be required only in very exceptional circumstances.

Microbiological Tests

Tests for infective agents reveal the pathogens in most of the cases. In simple pleural effusion direct smear for AFB is often negative, but in tuberculous empyema AFB may be numerous.

Pleural Biopsy

When the diagnosis of pleural disease is still in doubt, histological and microbiological studies can be undertaken with pleural biopsy specimens. Biopsy is better performed by the specialist. In some centers, biopsy is done along with the first pleural aspiration itself.

THORACOSCOPY

When pleural lesions have to be visualized *in situ*, the surface of the pleura can be inspected using a thoracoscope after producing a pneumothorax. Biopsy from abnormal areas can be done. This increases the accuracy of diagnosis. Open lung biopsy is also done at times after doing thoracotomy.

PULMONARY FUNCTION TESTS

For purposes of testing, respiratory function may be divided into its three gross components:

1. Ventilation
2. Vascular perfusion and
3. Diffusion of gases across the alveolocapillary membrane.

Ventilation

The static lung volumes such as tidal volume (VT), vital capacity (VC), inspiratory reserve volume (IRV) and Expiratory Reserve Volume can all be determined by spirometry, for which computerized instruments are available (Figs 13.18 and 13.19).

The state of arterial and venous systems can be studied by arteriography and venography using contrast agents. The several procedures include pulmonary artery angiography, angio cardiography, aortography, bronchial arteriography, superior vena cava angiography and azygography. Digital subtraction angiography (DSA) gives much better images of the vascular tree after removing the interference caused by bony and other structures.

Diffusion of oxygen and carbon dioxide across the alveolocapillary membrane is assessed by blood gas studies. Impairment of gas transfer across these alveolocapillary membrane is referred to as alveolocapillary block. Diffusion capacity across the alveolocapillary membrane is estimated by diffusion studies using different gases, e.g. carbon monoxide.

A sound knowledge of respiratory function tests is absolutely essential for the proper management of postoperative patients, post-traumatic conditions, poisoning and others. Monitoring artificial ventilation depends to a great deal on these studies. The physician and anesthetist managing intensive care wards (intensivists) should be fully conversant with all the pulmonary function test.

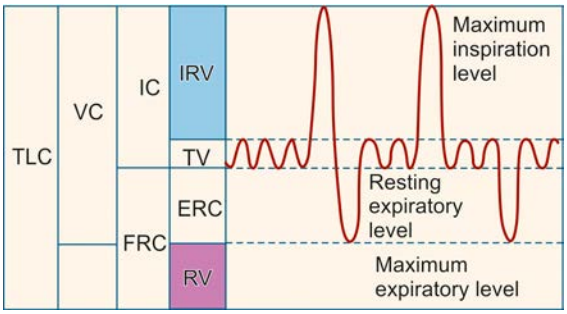


Fig. 13.18: Showing lung capacities by spirometry

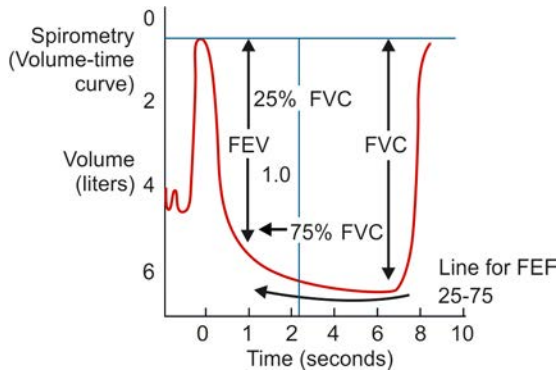


Fig. 13.19: Spirometry volume-time curve

Indications for Respiratory Function Tests

1. To assess the severity of damage caused by acute and chronic diseases which affect the respiratory system primarily or secondarily.
2. To determine the need for ventilatory support as an emergency life-saving or long-term measure.
3. For proper management of the cardio-respiratory function in intensive care facilities.
4. For instituting appropriate drug therapy, e.g. a patient with asthma who shows reversible airway obstruction responds well to inhalation of salbutamol and corticosteroids, whereas another patient with permanent airway obstruction as in emphysema does not respond quite well to these drugs.
5. For assessment during follow-up.

Selection of Respiratory Function Tests

Studies of Ventilation

Indications: Obstructive airway disease, bronchial asthma, chronic bronchitis with emphysema, pleural diseases, respiratory paralysis and others.

Studies of Arterial Perfusion of the Lungs

Indications: Suspected pulmonary embolism or multiple infarction, pneumonias, malignancy.

Studies on Diffusion of Gases Across the Alveolar Membrane

Indications: Alveolocapillary block syndromes such as pulmonary interstinal fibrosis, diffuse hyaline membrane disease in newborns, adult respiratory distress syndrome and others.

Studies of Ventilatory Function

Clinical Assessment of Ventilation

Capacity to narrate the history uninterruptedly without dyspnea suggests that the vital capacity is not dangerously low.

Making the patient blow out a lighted candle kept 30 cm away gives some idea about his expiratory capacity. If he can count loud up to 20 in a single breath after a deep inspiration it suggests that the vital capacity is around 2 L or more.

Anoxia due to respiratory failure leads to mental confusion and obtundation. As the condition worsens, flapping tremors develop. Retention of carbon dioxide leads to peripheral vasodilation, headache due to rise in intracranial tension, and even papilledema. Chronic hypoxemia leads to secondary polycythemia.

Investigations

The common parameters to study ventilatory function are:

1. Tidal volume
2. Vital capacity
3. Residual volume
4. Forced vital capacity (FVC)
5. Forced vital capacity in one second (FEV_1)
6. Peak expiratory flow rate (PEFR).

Computerized equipment is available to study these functions. Tidal volume and vital capacity are reduced in mechanical defects of ventilation.

Residual volume is increased in emphysema and chronic obstructive airway disease.

FVC and FEV_1 are both reduced in the same proportion in restrictive lung diseases, whereas FEV_1 is reduced far out of proportion to FVC in obstructive airway disease (Table 13.4). Normally $FEF_{(25-75\%)}$ is 80% of FVC. If this falls below 70% it indicates obstruction of small airways.

Forced expiratory flow 25 to 75% ($FEF_{25–75\%}$): This is the average rate of flow during the middle half of EFV. This is also called maximum *mid-expiratory flow rate.* FEV_1 25 to 75% is indicative of the status of medium sized airways.

Peak Expiratory Flow Rate

Peak expiratory flow rate (PEFR) is the maximum flow rate attainable at any time during an FEV and is recorded as liters per minute. Wright's peak expiratory flow meter is used to measure PEFR. At present, several bed side peak expiratory flow meters are available. The patient is made to breathe out with maximum force into the instrument, after taking a full inspiration. The PEFR is read on the instrument. Results are compared with norms prepared on normal controls according to age, height and sex. The PEFR is considerably reduced in obstructive airway disease.

Table 13.4: Differences between obstructive and restrictive lung diseases

Restrictive diseases e.g. Pneumoconioses, pulmonary fibrosis	*Obstructive diseases e.g. Bronchial asthma, emphysema, chronic bronchitis*
1. FVC and FEV_1 are reduced proportionately	FEV_1 is reduced much more than FVC
2. FEV_1 x 100 will be more than 75% FVC	Less than 75%
3. Residual volume is normal	Increased
4. PaO_2, may be decreased but $PaCO_2$, may not be raised	PaO_2, is reduced and $PaCO_2$, is increased

Functional residual capacity (FRC) and residual volume (RV) have to be measured indirectly because air occupying the residual volume cannot be removed from the lungs during life. For this, dilution studies using inert gases like nitrogen or helium are used.

Except the determination of PEFR all the other tests can be done only in laboratories specifically equipped for the purpose.

Perfusion Studies

Pulmonary vessels can be visualized by pulmonary angiography. Isotope studies using labeled macro-aggregated albumin reveals the state of pulmonary vasculature and shows up the unperfused areas.

Ventilation studies using isotope labelled gas xenon reveal the extent of ventilation. When perfusion and ventilation scans are combined, the disparity between ventilation and perfusion will be brought out, and unperfused, but ventilated areas can be mapped out.

Blood Gas Studies

Partial pressure of arterial oxygen (PaO_2) and carbon dioxide ($PaCO_2$) are estimated. ***PaO_2 in normal young adults is between 85 mm to 100 mm Hg. The term arterial oxygen saturation (SaO_2) indicates the amount of oxygen in milliliters held in combination with hemoglobin, expressed as a percentage of maximum amount of O_2 the***

hemoglobin can hold. The SaO_2 value corresponding to PaO_2 of 95 ± 5 mm Hg in a normal young adult is 97%. ***Arterial carbon dioxide is expressed only as its tension***. Normal $PaCO_2$ is 40 ± 2 mm Hg. In respiratory failure, PaO_2 falls and $PaCO_2$ rises. The levels of these gases in blood depend upon the type of respiratory failure. All diseases which lead to hypoventilation, diffusion defects and ventilation perfusion abnormalities decrease PaO_2. The PaO_2 may fall to levels as low as 40 mm Hg in both obstructive and restrictive lung diseases. Conditions associated with alveolar hypoventilation such as asthma, chronic bronchitis and emphysema lead to rise in $PaCO_2$ as well.

Major causes of hypoxemia are:

1. Reduction in oxygen content of inspired air
2. Generalized hypoventilation
3. Ventilation perfusion imbalance
4. Resistance to diffusion of gases across the alveolocapillary membrane, e.g. ARDS (Acute respiratory distress syndrome)
5. Right to left shunt occurring in congenital heart diseases.

Pulse oximeter is the instrument used to sense the content of oxygen in peripheral blood. Level of arterial carbon dioxide (CO_2) represents the balance between CO_2 production and CO_2 elimination.

Acid base balance: This gets deranged in both respiratory failure which causes *respiratory acidosis* and hyperventilation which causes respiratory *alkalosis.*

Monitoring of acid base balance and calculation of the *anion gap* are of utmost importance for proper management of acute and chronic respiratory failure due to all causes. *This is especially* so *if the patient is on assisted ventilation.*

Respiratory acidosis: This is acidosis developing as a result of failure of the lung to remove carbon dioxide from the circulation. In acidosis the pH is < 7.35. The parameters that are estimated include pH, PaO_2, $PaCO_2$ and plasma bicarbonate (HCO_3). Normal values are:

pH	7.35-7.45
$PaCO_2$	35-45 mm Hg
PaO_2	95-100 mm Hg
HCO_3	22-26 mEq/L

In acute respiratory acidosis, for every 1mm rise in $PaCO_2$ the pH falls by 0.008. On the other hand, in chronic respiratory acidosis, for every 1 mm rise in $PaCO_2$ the pH falls by only 0.003.

Respiratory alkalosis: This is alkalosis developing as a result of excess blowing out of carbon dioxide occurring in hyperventilation. In acute respiratory alkalosis for every 1mm fall in $PaCO_2$ the pH rises by 0.008. In chronic respiratory alkalosis, for every 1mm fall in $PaCO_2$ the pH rises only by 0.017. For every 1mEq/L fall in HCO_3 the corresponding fall in $PaCO_2$ is 1.2 mmHg.

Arterial plasma bicarbonate is 24 ± 2 mEq/L. Arterial blood pH is 7.40 ± 0.02. Acidosis leads to fall in pH and alkalosis to rise in pH (Table 13.5).

Method of Blood Collection for Arterial Gas Studies

A sample of blood is obtained by femoral artery or radial artery puncture using a heparinized syringe and the specimen should be sent without contact with atmosphere by sealing the needle tip and packed in ice.

Diffusion Studies

The diffusion of gases across the alveolocapillary membrane can be studied using carbon monoxide.

Respiratory failure is defined as the condition is which the PaO_2 is below 60 mm Hg and/or $PaCO_2$ above 49 mm Hg. In all types of respiratory failure there will be hypoxia. In normocapneic failure the $PaCO_2$ will be normal or below normal while in hypercapneic failure, the level of carbon dioxide also will be elevated.

Table 13.5: Biochemical differentiation between different types of acidosis and alkalosis

	Acidosis		*Alkalosis*	
	Metabolic	*Respiratory*	*Metabolic*	*Respiratory*
pH	Below 7.35	Below 7.35	Above 7.45	Above 7.45
PaO_2	Normal	Reduced	Normal	Normal
$PaCO_2$	Low	Elevated	Normal	Low
Respiration	Kussmaul's respiration	Slow and shallow	Normal	Low
Plasma (HCO_3)	Low	Normal or raised	Increased	Reduced

SECTION

6

Cardiovascular System

CHAPTER

14 General Considerations

KV Krishna Das, K Suresh

General considerations, Sequence of cardiac contraction, Arterial supply of heart, Nerve supply, Arterial blood pressure, Heart failure, Patterns of cardiovascular diseases seen in India

GENERAL CONSIDERATIONS

The adult human heart weighs 250 to 350 g. Sixty percent of the weight of the heart is constituted by the left ventricle. The left ventricle is 1 to 1.5 cm in thickness, the right ventricle is about 0.5 cm thick.

The intrinsic properties of cardiac muscle include excitability, contractility, rhythmicity, conductivity and distensibility. In normal hearts, increase in fiber length by distension leads to increase in force of contraction. This is Starling's law. When the heart muscle is diseased, this relationship is deranged. Energy for the myocardium is derived from the metabolism of free fatty acids, glucose, lactate, pyruvate and ketoacids. Heart uses 8 to 10 mL of oxygen per minute. The myocardial oxygen demand during systole is three times that during diastole. Both systolic contraction and diastolic relaxation are active energy dependent processes and when the heart muscle is diseased, both these functions may be deranged in varying degrees.

Stroke Volume, Cardiac Output and Cardiac Index

Stroke volume is the amount of blood ejected by the ventricles during each cardiac systole. It ranges from 65 to 75 mL. Cardiac output is the total amount of blood ejected by each ventricle per minute and it is the product of heart rate and stroke volume. In a healthy individual, it is around 5 to 6 liters. **Cardiac index** is the term denoting the output of each ventricle per minute per square meter of body surface area. Normal cardiac index is 3.4 L/m^2/ min (range 2.8–4.2). Cardiac output is governed by several factors such as effective venous return, heart rate, distensibility of the ventricles to receive blood in diastole (i.e. compliance), contractile force, obstruction to atrial or ventricular outflow and blood pressure. In health, the cardiac output can be increased to 20 L or more during exercise or emotional reactions. This is achieved by increasing the heart rate (acceleration) and contractile force (augmentation).

Conditions Causing Increased Cardiac Output

Exercise, emotional excitement, fever, thyrotoxicosis, anemia, pregnancy, beriberi, Paget's disease of bone, A-V malformations.

Conditions Causing Decreased Cardiac Output

1. Reduction in venous return into the atria as in hypovolemic shock.
2. Extreme tachycardia above 150/mt—the diastolic interval is shortened so that ventricular filling is reduced.
3. Extreme bradycardia—heart rate below 40/minute.
4. Weakness of myocardial contraction as in myocarditis, cardiomyopathy, cardiac failure and cardiogenic shock.
5. Anatomical or functional obstruction to inflow or outflow from cardiac chambers as in valvular heart diseases.

6. Arrhythmias such as atrial fibrillation. The booster effect of atrial contraction on ventricular filling is abolished.

SEQUENCE OF CARDIAC CONTRACTION

When the heart rate is 70 to 80/ minute, each cardiac cycle lasts for about 0.8 sec. The atria contract for 0.1 sec preceding ventricular contraction. Atrial diastole lasts for 0.7 sec during which time venous blood freely flows into the atria to fill them. Blood flow from atria to ventricles starts as a passive process beginning with the opening of the A-V valves in ventricular diastole. Initial phase of ventricular filling is rapid, later it slows down. Atrial systole helps to pump blood actively into the ventricles and this distending force on the ventricles acts as a booster for ventricular contraction. Atrial systole is not absolutely essential for ventricular filling, but its absence, as is seen in atrial fibrillation, leads to fall in cardiac output. This effect is clinically more pronounced in a diseased heart with anatomical or functional abnormalities.

Ventricular systole takes 0.3 sec and diastole 0.5 sec. The first event in ventricular systole is closure of A-V valves and this coincides with the first heart sound. The initial part of ventricular systole is isovolumetric contraction, with both A-V and semilunar valves closed. During this period intraventricular pressures work up and when they reach the diastolic pressures in the aorta and pulmonary artery, the semilunar valves open and ventricular ejection starts. The rate of ejection increases during midsystole and when 65 to 75% of ventricular blood is ejected, the rate of ejection comes down, and the semilunar valves close a bit later. This coincides with the second heart sound which marks the onset of diastole. Initial phase of relaxation is isovolumetric relaxation with both A-V valves and semilunar valves remaining closed. During this phase, the intraventricular pressure drops. The A-V valves open when the ventricular pressure falls below the atrial pressure to allow rapid ventricular filling. The rate of ventricular filling slows down as the flow proceeds and is augmented by atrial contraction just before the first heart sound.

ARTERIAL SUPPLY OF THE HEART

Blood supply to the myocardium is derived from the right and left coronary arteries, arising as the first branches of the aorta. They fill during diastole and the coronary blood flow is lesser during systole. Right coronary artery supplies right atrium, right ventricle, posterior aspect of interventricular septum and posterior wall of left ventricle. In addition, it supplies the SA and AV nodes and therefore occlusion of this artery leads to arrhythmias. The coronary artery which supplies the crux of the heart posteriorly and gives rise to the posterior descending artery is the dominant one. In the majority the right coronary artery is dominant. Left coronary artery supplies the left atrium, anterior part of the septum, and anterior and lateral parts of left ventricle. Major portion of the left ventricle is supplied by the left coronary artery and therefore total occlusion of this artery leads to major left ventricular infarction.

The arteries enter from the outer surface of the heart and the branches pass inwards. The epicardial aspect of the myocardium is better perfused than subendocardial region. Arterial blood flow to the myocardium is 72 to 82 ml/100 g/minute. There is no free communication between the branches of the two coronary arteries. Occlusion of a major branch leads to irreversible myocardial necrosis within six hours. In chronic ischemic heart disease some degree of collateral circulation develops and protective adaptation may occur.

The inside of the heart is lined by endocardium which is reflected on to the valves. The A-V valves are held on their ventricular aspect by the chordae tendinae of the papillary muscles, which also contract during systole, thereby preventing prolapse of the valve cusps into the atria. Dysfunction of the papillary muscles results in mitral incompetence.

The pericardium covers the outer surface of the heart. Between the visceral and parietal layers there is just enough fluid for lubricating the surfaces.

NERVE SUPPLY

Nerve supply to the heart is derived from the autonomic system which supplies the conducting system as well as muscle fibers. Vagus is the parasympathetic component. It supplies cholinergic parasympathetic fibers mainly to SA and AV nodes through M_2 muscarinic receptors. It reduces the rate of SA node and increases the refractory period.

Sympathetic fibers are derived from the cervical and upper thoracic ganglia. B_1 receptors predominate in the heart. Both adrenaline and noradrenaline have

positive inotropic (i.e. increasing force of contraction) and chronotropic (i.e. increasing rate) effects. B_2 receptors predominate in vascular smooth muscle.

Under basal conditions vagal influence predominates. The cardiac muscle is capable of initiating and maintaining contraction and rhythm as its intrinsic property, even when denervated.

ARTERIAL BLOOD PRESSURE

Normal systolic levels in different age groups:

Neonates	40 mm Hg
Infants aged 2 weeks	70 mm Hg
Children up to 12 years	105 mm Hg
Above 17 years	120 mm Hg

Blood pressure in the cardiac chambers:

Right atrium	3-7 mm Hg
Right ventricle	25/0 mm Hg
Left atrium	8-13 mm Hg
Left ventricle	120/0 mm Hg

HEART FAILURE

Heart failure is the condition in which the heart is not able to supply adequate blood to meet the metabolic demands of the body. This may result from reduction of cardiac output below normal (low output heart failure) or increase in demand far exceeding the capacity of the heart, even though the cardiac output is still above normal (high output failure). Mitral stenosis, myocarditis, hypertension and ischemic heart disease lead to low output cardiac failure. Thyrotoxicosis, pregnancy and cor pulmonale may give rise to high output cardiac failure.

Heart failure may develop gradually as in hypertension or cardiomyopathy, or abruptly as in acute myocardial infarction. When the development of heart failure is gradual the reserve capacity of the heart is affected first and symptoms are seen only on exertion, but with progressive fall in cardiac output symptoms occur at rest as well. Acute left sided heart failure leads to acute pulmonary edema. Acute right ventricular failure leads to systemic venous congestion.

PATTERN OF CARDIOVASCULAR DISEASES IN INDIA

Cardiovascular diseases account for over two million deaths annually in India. Heart disease accounts for 6 to 8% of the total medical admissions in any general hospital. Hence, in terms of mortality and morbidity cardiovascular disease is a major problem in India.

In children below the age of 10 years, congenital heart disease (CHD) predominates. The approximate prevalence of congenital heart disease is 6 to 8 per 1000 live births. Acyanotic CHD (65–70%) is much more common than cyanotic CHD (30%). Among the acyanotic CHD, bicuspid aortic valve, ventricular septal defect, patent ductus arteriosus and atrial septal defect are the most common. Among the cyanotic type, tetralogy of Fallot is most frequent. Rheumatic fever and acute carditis are also seen in this age group.

In children above the age of 10 years rheumatic valvular heart disease and congenital heart disease are more common. The approximate prevalence of rheumatic fever/ rheumatic heart diseases among school children shows marked regional variation and ranges from 1 to 2% in urban centers as compared to 6 to 7% in the rural North India. Apart from acute rheumatic carditis, chronic valvular lesions also develop in this age group. The course of rheumatic carditis is accelerated in India compared to the West, and so rheumatic valvular lesions are seen even at much younger ages. Mitral regurgitation is the most common lesion seen in children, followed by mitral stenosis with or without incompetence, aortic incompetence, aortic stenosis and rarely tricuspid valve lesions as the usual rheumatic sequelae.

Pericarditis is seen in all age groups. In children and young adults, viral pericarditis, dyscollagenosis, tuberculous pericarditis and other inflammatory causes are more frequent. Uremic pericarditis may occur in all age groups. In the age group above 50 years, ischemic pericarditis and malignant lesions predominate.

In the elderly age groups, ischemic heart disease, hypertension, hypertensive heart diseases and cor

pulmonale top the list and they account for most of the cardiac morbidity.

The prevalence of ischemic heart disease in India varies from 5 to 7% in the rural areas to 10 to 12% in urban population.

Hypertension is very prevalent. The limited surveys give figures as low as 5% among tribal populations, between 20 to 30% in rural areas and as high as 30% in the urban population. Hypertensive heart disease and strokes are common.

Many studies report the prevalence of abnormal blood lipid levels (cholesterol, triglyceride, low density lipoproteins—LDL), lipoprotein-A (LpA) and others in the rural (20–30%) and urban (30–40%) population. These predispose to atheroma and ischemic heart disease.

Diabetes mellitus is another coronary risk factor with increasing prevalence both in urban and rural populations at all ages and varies between 20 to 30% in Indians.

Smoking also is quite common especially in the males with a prevalence ranging from 25 to 40% in many studies. The prevalence of smoking in women is also increasing.

Arrhythmias are common in all age groups. Ischemic heart disease, rheumatic heart disease, sick sinus syndrome and drugs like digoxin account for the majority.

All types of heart diseases described in other parts of the world are present in India. In addition some cardiovascular problems are more prevalent, for example, endomyocardial fibrosis, aorto-arteritis, thromboangiitis obliterans and poisoning by cardiotoxic vegetable poisons such as Cerbera odollam, Nerium oleander and Cleistanthus collinus leaf.

Clinically diagnosed pulmonary embolism is less common and the prevalence reported from autopsied cases also seems to be less in India. Infective endocarditis is not uncommon. Very often this supervenes on congenital and acquired heart lesions. Mitral valve prolapse and bicuspid aortic valve are two common conditions that predispose to infective endocarditis in apparently healthy persons.

Cardiac surgery is now being done in many centers, and an increasing number of patients may present with post-cardiac surgery problems. These include congenital heart diseases—surgically repaired or palliated, prosthetic valve dysfunction, prosthetic valve endocarditis and post-coronary artery intervention problems.

CHAPTER

15 Examination of the Cardiovascular System

KV Krishna Das, K Suresh

Dyspnea, Chest pain of cardiac origin, Palpitation, Hemoptysis, Syncope, Edema, Cyanosis, Fatigue, Cough, Symptoms related to arteries, Symptoms related to veins, Past history, Physical examination-general examination, Examination of pulse, Examination of jugular veins, Examination of chest, Palpation of the precordium, Percussion of precordium, Auscultation of the heart and blood vessels, Recording of blood pressure

DYSPNEA

Dyspnea is defined as an uncomfortable subjective awareness of one's own breathing. Dyspnea is a limiting factor of physical activity caused by very strenuous or unaccustomed exertion even in healthy people. This is not abnormal. When it occurs at rest or at levels of activity which are usual to the patient, it is considered abnormal. Dyspnea is a common manifestation of cardiac and pulmonary diseases. Cardiac causes for dyspnea are detailed below.

In patients with heart disease, dyspnea indicates pulmonary venous congestion. Elevation of pulmonary venous pressure usually results from either left ventricular failure or mitral stenosis.

Left ventricular failure (LVF) is the most common cause of pulmonary venous congestion. Conditions that cause LVF include systemic hypertension, coronary artery disease, cardiomyopathy, myocarditis, valvular heart diseases especially mitral regurgitation and aortic valve lesions. LVF leads to rise of the left ventricular end diastolic pressure which is transmitted backwards to the left atrium and pulmonary veins. This leads to pulmonary venous congestion. When pulmonary venous pressure exceeds 22 mm Hg, dyspnea occurs even at rest. If the resting pulmonary venous pressure is lower, dyspnea occurs only on exertion which precipitates left ventricular dysfunction.

In mitral stenosis, mechanical obstruction to atrial emptying causes rise in left atrial pressure which is transmitted retrograde to the pulmonary veins. Other rare causes of obstruction to left atrial outflow include left atrial myxoma and ball valve thrombi, cor triatriatum and supramitral rings. Rarer anomalies such as stenosis of the pulmonary veins can also cause pulmonary venous congestion and dyspnea.

Occasionally patients with ischemic heart disease may experience exertional dyspnea instead of pain. In such cases dyspnea is an anginal equivalent and is due to ischemia causing transient left ventricular dysfunction. The dyspnea in most of these conditions is gradual in onset and progressive. Acute or sudden onset of dyspnea suggests acute pulmonary edema, acute pulmonary embolism, pneumothorax or an acute obstruction to airways. In a patient with ischemic heart disease, sudden exacerbation of dyspnea should suggest acute myocardial infarction or its complications such as acute pulmonary edema, acute mitral regurgitation, ventricular septal rupture or pulmonary embolism. In a patient with mitral stenosis, it often indicates the onset of atrial fibrillation or pulmonary embolism.

For purposes of uniformity in quantitation, the New York Heart Association (NYHA) classification of functional status is commonly used to describe symptoms such as dyspnea, chest pain, fatigue and palpitation.

NYHA Functional Classification

Class I	Dyspnea occurring at heavy, but accustomed activity
Class II	Dyspnea occurring on moderate exertion
Class III	Dyspnea during mild exertion or during daily routine activities
Class IV	Dyspnea even at rest.

Paroxysmal Nocturnal Dyspnea

Paroxysmal nocturnal dyspnea (PND) term refers to the sudden onset of severe dyspnea occurring in a cardiac patient during sleep at night. Though classically described as nocturnal, it can also occur during day if the circumstances permit. The patient who goes to sleep comfortably is awakened suddenly within 1 to 2 hours by acute shortness of breath and cough with frothy blood stained sputum. He is apprehensive and distressed. He gets relief by sitting up, reclining in a chair or even walking to an open window to get fresh air. These attacks are highly suggestive of severe pulmonary venous congestion secondary to left ventricular failure or mitral stenosis.

Mechanisms of PND

- When the patient assumes recumbency, the increase in venous return from the lower limbs combined with the reabsorption of the edema fluid leads to increased central blood volume. In the failing heart, the left sided chambers cannot cope up with this increased inflow and this leads to pulmonary congestion.
- Diurnal variations in the secretion of ADH cause fluid retention nocturnally during sleep, worsening the pulmonary congestion.
- Diminished sympathetic nervous system activity during sleep leading to diminution of the catecholamine support to the failing myocardium at night is another mechanism.
- Association with the REM phase of sleep and proneness for arrhythmias is this period may contribute to pulmonary congestion and PND. These are some of the reasons for worsening of dyspnea at night.

PND has to be distinguished from acute attacks of bronchial asthma.

Dyspnea due to cardiac causes	*Dyspnea due to respiratory causes*
Primary mechanism is pulmonary congestion	Primary mechanism is bronchoconstriction
Dyspnea often gets relieved on assuming the erect posture	Dyspnea often persists even after assuming the erect posture
Past history of cardiac illnesses or other cardiac symptoms like palpitation or angina	Past history of asthma, COPD and respiratory symptoms such as cough or wheeze
Physical examination reveals cardiomegaly, S_3 gallop, cardiac murmurs and basal crepitations	Physical examination reveals marked expiratory wheeze and rhonchi

Note: At times the distinction between cardiac and respiratory causes for acute dyspnea may not be clear cut. Rarely these conditions may also coexist

Orthopnea

This is the condition in which the patient has dyspnea on lying supine, but gets relief in the sitting or propped up position. Increased venous return from the lower limbs in the supine posture precipitates cardiac decompensation and pulmonary venous congestion in the presence of left ventricular failure. Moreover the pressure of the abdominal viscera on the diaphragm in the supine posture contributes to the dyspnea. However, patients with respiratory ailments such as bronchial asthma and emphysema also prefer the sitting position since the ventilatory mechanics are more efficient in the upright or sitting position.

CHEST PAIN OF CARDIAC ORIGIN

Chest pain is an important symptom of cardiac diseases especially in ischemic heart disease, which is more common above the age of 45 years but no age is exempt. Chest pain occurring in age groups below 30 years is less likely to be of ischemic heart disease. Chest pain due to cardiac causes has to be differentiated from noncardiac chest pain. Endocardium is not pain sensitive, but diseases affecting the myocardium, especially ischemia and pericarditis present with chest pain. In myocardial ischemia, accumulation of metabolic products stimulates the local nerve endings. Afferent impulses are carried to the lower cervical and first thoracic ganglia through the cardiac sympathetic nerves. Referred pain is felt diffusely over the dermatomes supplied by these ganglia.

Primary reduction in coronary arterial blood flow occurs when the coronary arteries are narrowed,

most frequently due to atherosclerosis. Critical obstruction (> 70% of the lumen) of the major coronary arteries leads to myocardial ischemia. Often in addition to the major arteries distal branches may also be occluded.

Less commonly primary non-atherosclerotic involvement of the coronary arteries may occur in various forms of vasculitis such as polyarteritis nodosa and Kawasaki's disease and also in thromboangiitis obliterans.

In addition to the primary lesions in the blood vessels, other precipitating factors worsen ischemia. These include exertion, emotional disturbances, tachycardia, anemia, high altitude and others.

Angina may also result from primary reduction of coronary blood flow without any increase in myocardial oxygen demand, as is seen in coronary artery spasm. Rarely under exceptional circumstances such as severe emotional stress, it can develop even on otherwise normal coronary arteries.

The most common clinical expression of myocardial ischemia is "angina pectoris" literally meaning "chest pain". When it occurs on exertion it is known as exertional angina. Most often the quality of pain is described as compressive or crushing in the retrosternal region. It is vague in nature and imprecise to be located exactly. The chest pain is associated with pain over other sites. In the order of frequency, the classical sites of radiation are the front of the neck, sides of the neck, jaw, medial aspects and fingers of both upper limbs and the back of the chest. It is not uncommon for the pain to start in the epigastrium and either remain there or spread to the central chest and other areas of reference. Occasionally, the pain may start in an upper limb, jaw or neck and then migrate to the central chest. In many cases the pain may be associated with sweating, dyspnea, palpitation, dizziness and a feeling of impending death ("angor animi"). It should be remembered that cardiac pain may occur very atypically in quite unexpected situations and therefore it should be a golden rule to rule out cardiac ischemia by electrocardiogram in all situations where ischemic heart disease is a possibility. This would help to avoid unexpected mortality and also to institute early reperfusion therapy. The severity of pain as expressed by the patient and the severity of the lesion may not directly correlate.

Typical effort angina is precipitated by exertion and relieved promptly by rest within seconds or minutes and usually it does not last more than 10 minutes. It is also relieved by the administration of vasodilators such as nitrates, within 3 to 5 minutes. The classical description of angina holds good only in 30 to 50% of cases. In the others, the pain is atypical, and in many, myocardial ischemia may be totally silent (silent myocardial ischemia, e.g. diabetes, old age).

Prinzmetal's Angina (Syn: Variant Angina)

In this variant of angina, coronary artery spasm plays the major role in precipitating angina. Spasm may occur *de novo*, but it supervenes most frequently on diseased coronary vessels. The pain is similar to effort angina, but the clinical picture differs in the following points.

1. Also common in women.
2. It occurs at rest, usually at night during sleep, or early morning.
3. The duration is prolonged.
4. Serious arrhythmias may develop.
5. There may be other evidence of vasospasm such as migraine or Raynauds phenomenon.
6. Response to therapy with sublingual nitrate is unsatisfactory in many cases.

At times angina may occur also in conditions where the coronary arteries are not primarily at fault, e.g. aortic stenosis and incompetence, syphilitic aortitis, aortic aneurysm, and coronary artery embolism. In aortic stenosis and other conditions leading to ventricular outflow obstruction, cardiac hypertrophy develops, thereby increasing the oxygen demand. This factor, combined with reduced perfusion pressure in the coronary arteries, results in angina. Such angina may also complicate aortic incompetence, syphilitic aortitis (due to narrowing of the coronary ostia) and coronary emboli occurring in infective endocarditis.

Stable Angina and Unstable Angina

Many anginal patients may carry on their usual activities for several years with some moderation in lifestyle and treatment with nitrates or other cardiac drugs. This condition is termed "chronic stable angina". In some, the severity and frequency of angina may even reduce considerably with time due to establishment of collateral circulation.

Patients presenting with new onset angina of less than two months duration or progressive aggravation of symptoms in the recent past (within two months), or angina following an acute myocardial infarction are considered to have "unstable angina". Prognosis of unstable angina is worse since the majority of such patients have severe and progressive coronary artery disease which may lead to acute myocardial infarction or fatal arrhythmias. The Braunwald's classification of unstable angina helps in understanding the different types of unstable angina.

A patient with chronic stable angina should be considered to have gone into the unstable phase when he develops any of the following features within the preceding two months:

1. Increased frequency, severity, or duration of pain.
2. Angina occurring with decreasing levels of exertion.
3. Pain occurring even at rest.
4. Alterations in the pattern or characteristics of pain.
5. Decreased response to nitrates and progressively greater demand for their use.

Patients with unstable angina have to be managed with greater care to prevent major cardiac events such as acute myocardial infarction, fatal ventricular arrhythmias or sudden death.

The Syndrome of Acute Myocardial Infarction

Acute myocardial infarction (AMI) is characterized by intense retrosternal chest pain, often starting at rest and becoming progressively more severe and unbearable, with the classical radiation and other associated symptoms. The sites of radiation are:

1. The upper part of the chest and neck, upto the jaw.
2. Left shoulder and inner aspect of left arms and hand.
3. Right shoulder and right hand.
4. Back of the chest to the scapular region.
5. Epigastrium and upper abdomen.
6. Or atypically to any other part of the body.

The associated symptoms consist of sweating, vomiting and dyspnea. Patients with acute myocardial infarction usually complain of a premonitory feeling of impending death (angor animi). The pain persists for more than 30 minutes and is not generally relieved by nitrates. On account of wide awareness of heart attack among the general population, several patients come to hospital early, often within a few hours. But rarely the patient may present much later with pain of longer duration, because of its atypical nature or lack of awareness of the condition.

Acute myocardial infarction is due to the total occlusion of blood flow through a major epicardial coronary artery and this, in over 90% of instances is due to thrombus.

Patients presenting with myocardial infarction on the basis of the findings in the initial electrocardiogram are described as having STEMI (ST elevation myocardial infarction) and NSTEMI (Non ST elevation myocardial infarction). This is important for deciding on the mode of therapy and for triaging patients accordingly. Patients having STEMI should be channeled into the appropriate reperfusion strategy viz, thrombolytic treatment or primary angioplasty without any time delay. The concept of "***time is muscle***" highlights the importance of minimizing the time delay to maximize myocardial salvage.

The ***door to needle time*** is the time from the presentation of the patient to the emergency room to the initiation of the thrombolytic treatment. The ***door to balloon time*** likewise refers to the time from the presentation of the patient in the emergency room to the opening of the occluded coronary by balloon dilatation by primary angioplasty. Hospitals should streamline management protocols to ensure that the door to needle time and the door to balloon time are minimized to the fullest extent. In the majority of centers in India as well as across the globe, even today most patients with myocardial infarction are managed by thrombolytic treatment. However, in many countries and in centers with percutaneous intervention (PCI) capable cath labs the preferred mode of treatment for acute STEMI is balloon angioplasty.

Myocardial ischemia and/or infarction results in ventricular dysfunction or arrhythmias.

Ventricular dysfunction can vary from mild asymptomatic LV systolic or diastolic dysfunction to florid acute left ventricular failure, congestive heart failure or even cardiogenic shock. Arrhythmias include serious and life-threatening forms such as ventricular tachycardia, ventricular fibrillation or severe degrees of heart block and less malignant

arrhythmias such as atrial fibrillation, ectopic beats and lesser degrees of heart block.

It should be remembered that the classical description of the onset of myocardial infarction occurs only in one-third of the patients. ***In 30%, the pain may be atypical or may even be absent. It is therefore a golden rule in all cases of chest pain, however typical or atypical it may be, to record the electrocardiogram (ECG) to confirm or exclude the presence of myocardial ischemia. The ECG gives valuable information in over 80% of cases straight away.***

Ischemic heart disease is rare among normal women who have not attained menopause. Smoking, diabetes mellitus and menopause abolish this gender protection females have. Diabetic women, particularly smokers have a much higher risk of developing ischemic heart disease. Women attain the same risks for ischemic heart disease comparable to men during postmenopausal life.

Cardiac Pain: Nonischemic Causes

The pain of acute pericarditis is not related to effort, but is usually aggravated by deep breathing. It is felt as a superficial sharp pain confined to the precordium. Turning from side to side may aggravate the pain and leaning forward may give relief. In pericarditis resulting from infections, fever may be evident from the start. Sometimes the pain of pericarditis may closely resemble that of AMI and clinical distinction may be impossible. Moreover in many cases of AMI, acute pericarditis may develop as a complication and the two conditions may coexist. Development of effusion often mitigates the pain of acute pericarditis.

Aneurysms of the aorta may erode vertebral bodies and produce constant and severe pain lasting for months, referable to the chest or abdomen. Acute dissecting aneurysm of aorta produces tearing pain of dramatically sudden onset in the upper chest, posteriorly more often than anteriorly. The pain radiates along the great· arteries as the dissection extends into them even to the lower limbs.

Pain related to severe pulmonary hypertension may mimic angina pectoris or it may be a dull pain. Severe pulmonary hypertension occurs in mitral stenosis, Eisenmenger's syndrome, and primary pulmonary hypertension. The site of origin of pain may be the distended pulmonary artery or it may be due to right ventricular myocardial ischemia.

Pulmonary embolism is another condition causing chest pain, often associated with severe dyspnea and hypoxia with clear lung fileds. Chest pain occurs due to the moderate sized pulmonary infarcts which involve the pleura and the pain is often due to the pleurisy.

Other frequent causes of chest pain which mimic cardiac pain include anxiety neurosis, (cardiac neurosis or Dacosta syndrome, costochondritis, preherpetic neuralgia and pain referred from abdominal organs). Also refer Table 12.3 in Chapter 12 for further details.

Pain which is fairly localized, superficial, inframammary and in which the patient can often point to the site of pain often tends to be of non-cardiac origin. Such pain may also be variable in location, catching or pricking in nature, with no definite relation to effort. In many of them the pain is of long duration, often lasting for several years.

PALPITATION

Palpitation is an unpleasant subjective awareness of one's own heart beat. In normal individuals it occurs during vigorous exercise or emotional stress but it is short-lived.

Palpitation may result from tachycardia, severe grades of bradycardia, irregularity of cardiac rhythm or increased force of contraction.

Tachyarrhythmias are the most common cause of palpitation. Abrupt onset and cessation of the tachycardia are suggestive of paroxysmal tachy-cardias. Intermittent and irregular palpitation may be due to multiple ectopic beats, atrial fibrillation or atrial flutter. In those with ectopic beats, the unusually forceful heart beat that follows the long compensatory pause is felt as a thud or a quivering movement. Palpitation may occur in anxious individuals who have no organic heart disease. Such individuals tend to concentrate on the heart beat and thereby become aware of it.

When palpitation is associated with features of reduced perfusion to the brain such as dizziness, dimness of vision and syncope, the possibility of serious heart disease is high. If the patient has learnt to terminate an attack of tachycardia by inducing vagal stimulation by Valsalva maneuver, rubbing the

neck and eyes, or drinking ice cold water, it is indicative of paroxysmal atrial tachycardia. Cessation of paroxysmal atrial tachycardia, intermittent atrial fibrillation and atrial flutter are often accompanied by diuresis.

Bradyarrhythmias also can manifest as palpitation. In complete heart block since the heart rate is very slow, and diastolic interval is long, increased filling of the ventricle leads to increase in stroke volume and forceful contraction. This gives rise to palpitation. The patient may complain of regular forceful heart beats. In sick sinus syndrome brady and tachycardias produce palpitation.

Volume overload of the ventricles can cause palpitation due to the forceful contraction. Aortic or mitral regurgitation in which left ventricular stroke volume is increased and atrial septal defect in which right ventricular stroke volume is increased may present with palpitation as the main symptom.

HEMOPTYSIS

Cardiovascular diseases account for some cases of hemoptysis. Cyanotic congenital heart diseases, Eisenmenger's syndrome, and mitral valve disease contribute the majority. Pink frothy sputum is characteristic of acute pulmonary edema. The sudden elevation of pulmonary venous pressure causes transudation of fluid and oozing of blood into the alveolar spaces. When mixed with the alveolar air it gives rise to the characteristic pink and frothy appearance. Blood streaking of the sputum is also common in acute pulmonary congestion. As an early complication of rise in pulmonary venous pressure, the bronchopulmonary venous collaterals may rupture causing bleeding which is often mild and self limiting. Superadded respiratory infection leading to bronchitis also contributes to hemoptysis. Pulmonary thromboembolism leading to pulmonary infarction leads to frank hemoptysis associated with varying grades of dyspnea, and often pleuritic pain. Pulmonary apoplexy resulting from very massive bleeding can occasionally occur due to rupture of dilated and tortuous bronchial veins. Massive and fatal hemoptysis may also result from rupture of pulmonary arteriovenous fistula or aortic aneurysm eroding into a bronchus (*See* also Table 12.2).

SYNCOPE

Syncope is defined as transient loss of consciousness due to inadequate cerebral blood flow causing cerebral hypoxia. Since brain is the largest consumer of oxygen, and its oxygen need is the highest, reduction in arterial blood flow promptly manifests as syncope within seconds to minutes. Prolongation of ischemia beyond a few minutes results in irreversible neuronal damage—the syndrome of brain death.

The clinical picture is characterized by rapid onset of dizziness, dimness of vision, loss of tone and slumping to the ground in an unconscious state. This may be accompanied by vasomotor phenomena such as coldness of limbs and profuse sweating. The pulse may be rapid, slow or absent. Blood pressure is often very low. On assuming the recumbent posture cerebral flow improves and the patient recovers. If restoration of cerebral flow is delayed due to any reason, convulsions may develop.

Syncope may result from several cardiac and vascular disorders (Table 15.1). Cardiac syncope is usually abrupt in onset and recovery is also fast. Stokes-Adams attacks are seen commonly in complete heart block and in all higher grades of heart blocks. These are due to self-limiting episodes of ventricular fibrillation or asystole during which time there is no effective cardiac output. Left ventricular outflow obstructions like aortic stenosis, or hypertrophic obstructive cardiomyopathy, and severe mitral stenosis with pulmonary hypertension can

Table 15.1: Cardiovascular causes of syncope

1. Arrhythmias	*Bradyarrhythmias* Sick sinus syndrome - sinus arrest, SA blocks Complete heart block, other high grades of heart block, cardiac asystole *Tachyarrhythmias* Paroxysmal supraventricular tachycardias, atrial fibrillation with rapid ventricular rate, ventricular tachycardia, ventricular fibrillation
2. Mechanical causes obstruction to ventricular inflow or outflow restricting cardiac output	*Obstruction to ventricular outflow* Aortic stenosis, hypertrophic obstructive cardiomyopathy, pulmonary stenosis, severe pulmonary artery hypertension, pulmonary embolism *Obstruction to ventricular inflow.* Tight mitral stenosis, atrial myxoma, ball valve thrombus in atria
3. Other causes	Cardiogenic shock, cardiac tamponade postural hypotension, carotid sinus hypersensitivity, hypovolemic states vasovagal syncope (vasoreactive syncope)

cause syncope on exertion. In these conditions, the cardiac output remains fixed and the increased blood flow to the exercising muscles causes a transient relative diminution of cerebral blood flow leading to syncope. Postural hypotension, and hypovolemia resulting from dehydration, blood loss or shock can also cause syncope. Vasovagal attacks usually occur in response to emotional or painful stimuli. It is characterized by fall of blood pressure and an inappropriately low heart rate, and is accompanied by profound vasodilatation.

Assumption of supine posture may abort a vasovagal attack. Syncope resulting from leaning, bending or other postural variations should make one suspect a left atrial myxoma which obstructs the mitral orifice in these positions. Syncope associated with micturition or following prolonged coughing-referred to as micturition syncope or post-tussive syncope respectively, is due to a reduction in venous return to the heart.

Syncope preceded by chest pain may be the presenting symptom of acute myocardial infarction. Transient atrioventricular blocks and tachy-or bradyarrhythmias are not uncommon initial events in the evolution of inferior wall myocardial infarction.

Syncope may arise from obstruction to carotid or vertebral arteries or sudden changes in intra-cranial tension. This may be accompanied by other neurologic symptoms.

Another rare cause of syncope is hypersensitivity of the carotid sinus in which mechanical factors like pressure over the carotid sinus due to tight collars or even shaving can cause loss of consciousness. This may be of the cardioinhibitory type where syncope is due to bradyarrhythmias and can be treated by pacemaker implantation or the vasodepressor type where the syncope is due to hypotension and vasodilatation and does not respond to pacemaker therapy. Very often both mechanisms may coexist.

Pulmonary hypertension, Eisenmenger's syndrome, and cardiac tamponade can produce syncope at times, which is mostly related to exertion and is due to the fixed cardiac output. Postural hypotension if severe can also cause syncope.

Since syncope may be associated with convulsions, it is important to distinguish this from seizure disorders, especially grand mal epilepsy. The patient recovering from syncope is often able to narrate the incident whereas the one recovering from epilepsy is not. The main points of differentiation are listed in Table 15.2.

Table 15.2: Points to distinguish syncope from epilepsy

Clinical feature	*Syncope*	*Epilepsy*
Loss of consciousness	Occurs within seconds to minutes Dizziness	Occurs within a split second
Premonition	Blurring of vision, sweating	Aura may be present
Posture	Occurs during erect posture and is relieved in recumbent posture	Not related to posture
Fall	Often slumps to the ground	Falls heavily
Recovery of consciousness	Rapid, on adopting flat position	Passes through the classical stages postictal, unconsci-ousness may persist
Injuries	Usually absent	Injuries may be caused by fall, biting of tongue, etc.
Recall	Can recall history on recovery	Has no recall of what happened
Underlying pathology	Reduced blood flow to brain	Electrical discharge from abnormal focus

EDEMA

Right sided heart failure is accompanied by systemic venous congestion and peripheral edema, whereas left sided heart failure is accompanied by pulmonary venous congestion and pulmonary edema.

Dependent edema, particularly prominent towards evening is a characteristic symptom of congestive cardiac failure. The sequence of events is: (1) rise in jugular venous pressure, (2) enlargement and tenderness of the liver, and (3) dependent edema.

As the condition progresses, symmetric dependent edema sets in. This is preceded by weight gain of 3 to 4 kg due to water retention. Though the edema is predominantly over the dependent parts, with worsening of the condition, the edema may extend to the thighs, abdominal wall and face, particularly in children. Ascites may also develop. Similar distribution of edema can occur in cirrhosis of liver, but in cirrhosis, ascites is more prominent than peripheral edema. In chronic right sided heart disease such as tricuspid incompetence, constrictive pericarditis and right ventricular endomyocardial

fibrosis, chronic venous congestion of the liver leads to cardiac cirrhosis. In these conditions ascites tends to be more prominent than peripheral edema (*See* also Chapter 2 General Examination).

CYANOSIS

Cyanosis is bluish discoloration of lips, finger tips and mucous membranes due to increased levels of deoxygenated hemoglobin in the capillary blood above 5 g/dL. In congenital heart disease, cyanosis develops when the right to left shunt exceeds 25% of left ventricular output. Cyanosis is manifested from birth in conditions like transposition of great vessels and tricuspid atresia. Cyanosis setting in after six months of age is the picture in tetralogy of Fallot (TOF). Onset of cyanosis between 5 and 20 years is suggestive of Eisenmenger's reaction. When patent ductus arteriosus (PDA) goes in for Eisenmenger's reaction, differential cyanosis occurs, the lower limbs are cyanosed whereas the upper limbs are spared (*See* also Cyanosis in Chapter 2).

FATIGUE

Fatigue is a less specific symptom. In cardiac patients it may be the combined effect of the disease process aggravated by anxiety or depression. In patients with low cardiac output states, whether due to left or right heart involvement, fatigue may be the predominant symptom. Pulmonary stenosis and pulmonary hypertension may manifest as severe fatigue. In longstanding left ventricular failure, when right ventricular failure also develops, orthopnea and paroxysmal nocturnal dyspnea decrease, but symptoms like fatigue and weakness become more prominent. Fatigue caused by low output cardiac lesions is aggravated by exertion whereas fatigue caused by anxiety or depression is unrelated to exertion. Other common causes of extreme fatigue in cardiac patients are the use of diuretic drugs which deplete sodium and potassium, and antihypertensive drugs which cause marked fall in blood pressure.

COUGH

Cardiac lesions produce cough as a result of rise in pulmonary venous pressure, interstitial or alveolar edema and pulmonary infarction. Compression of left recurrent laryngeal nerve by the dilated pulmonary artery, enlarged left atrium caused by mitral stenosis and aneurysm of the aorta, may result in hoarseness of voice and cough. Persons receiving angiotensin converting enzyme inhibitors may develop troublesome cough as an adverse side effect. Patients with chronic venous congestion of lungs are prone to develop recurrent pulmonary infections which also contribute to the cough (*See* also Table 12.1 in Chpater 12).

SYMPTOMS RELATED TO ARTERIES

Gradual occlusion of arteries leads to intermittent claudication. This is the occurrence of cramp like pain over the muscles brought on by exertion and relieved by rest. As the occlusion becomes more severe, rest pain occurs. This is excruciating pain disturbing sleep. Infection in the limb worsens the pain. A common cause of occlusion of peripheral arteries is atheroma. This is often associated with atheroma of coronary and cerebral arteries as well. Thromboangiitis obliterans is very prevalent in India among smokers.

Arteritis occurring in polyarteritis nodosa and infective endocarditis, present as painful and tender nodules. Sudden occlusion of a major arterial trunk leads to intense pallor and coldness of the limb. If the circulation is not restored, gangrene follows.

SYMPTOMS RELATED TO VEINS

Venous occlusion leads to distal edema. Phlebitis or inflammation of the veins leads to painful tender linear swellings, usually in the thigh, calf, or axilla. The thrombosed vein can be palpated as a cord. Phlebothrombosis without inflammation may occur silently. Common sites are the calf veins and pelvic veins. Since the thrombus is free in the venous lumen, it is likely to embolise and lead to pulmonary embolism. Recurrent thrombophlebitis may be a symptom of malignant lesions, especially pancreatic cancer, and other forms of thrombophilia.

Varicose veins produce aching pain and distal edema, especially when the patient adopts the erect posture for prolonged periods. Later complications include eczema, ulceration and rupture of veins.

PAST HISTORY

In India, rheumatic fever is still common among the poor socioeconomic groups. In all cases of valvular heart disease, previous history of rheumatic fever should be enquired into.

Infective endocarditis supervenes on already existing cardiac diseases such as rheumatic and congenital lesions and insertion of prosthetic valves. Hence any patient with suspected infective endocarditis should have a history of structural heart disease enquired into.

Ischemic heart disease is more common in people with diabetes, dyslipidemia, obesity and hypertension. Sedentary habits, active and passive tobacco smoking, stress and diets high in saturated fatty acids, accelerate the development of atheroma and occlusive arterial disease. It is important to ask for history of diabetes mellitus, hypertension, prior ischemic heart disease, renal disease, and vascular disease—peripheral or cerebral—in any adult presenting with cardiovascular disease. Chronic kidney disease, especially microalbuminuria is recognized as an important cardiovascular risk factor today.

Nutritional disorders such as beriberi (aneurine deficiency) are associated with cardiomegaly and cardiac failure. Alcoholics who consume large quantities of alcohol may develop beriberi or alcoholic cardiomyopathy.

Family History

Rheumatic fever and beriberi tend to run in the same household due to similar environmental factors. Premature ischemic heart disease (below the age of 55 years in males and 65 years in females) may run in families. Ischemic heart disease in the young (below 40 years) may be caused by many risk factors and also familial hyperlipidemias. Hypertension is also more common among family members. Hypertrophic obstructive cardiomyopathy shows autosomal dominant pattern of inheritance. Conditions which predispose to sudden cardiac death such as long QT interval syndromes and Brugada syndrome also has a strong genetic basis.

Occupation

It is known that occupations which cause mental stress, at the same time reducing the opportunity for physical activity are associated with a greater risk of developing ischemic heart disease. Type A personality is also associated with higher risk of ischemic heart disease. Hence, ischemic heart disease is more frequent among business executives and doctors.

Drug History

Drugs like oestrogens, and testosterone lead to fluid retention.Sympathomimetic drugs such as ephedrine cause elevation of blood pressure. Antileukemic drugs such as daunorubicin cause myocarditis and delayed cardiomyopathy. Long-term use of appetite suppressant drugs such as fenoxetine, fenfluramine and others is associated with primary pulmonary hypertension and also incompetence of the aortic and mitral valves. Sibutramine should not be given to patients with ischemic heart disease or cardiac failure.

Obstetric History

Pregnancy, parturition and lactation cause heavy demands on cardiac function and so these are periods when an underlying heart disease deteriorates or becomes clinically evident for the first time. With successive pregnancies the cardiac status deteriorates. Puerperal cardiomyopathy is a rare form of heart disease seen during the later stages of pregnancy or during puerperium.

PHYSICAL EXAMINATION

General Examination

A detailed general examination with special reference to the following points should precede examination of cardiovascular system.

Growth and development: These are retarded in serious forms of heart diseases with major hemodynamic abnormalities. General stunting of growth may occur in cyanotic congenital heart diseases like Fallot's tetralogy or even in acquired heart diseases (rheumatic) with severe hemodynamic disturbances.

Congenital Abnormalities

These include polydactyly, accessory nipples, abnormalities of eyes and ears, abnormalities of limbs and other structures. These may be associated with congenital heart disease (Table 15.3).

Record of body weight maintenance or a weight chart is the easiest and most reliable method to detect accumulation of fluid in the body. In heart failure, one of the earliest abnormalities is the retention of sodium and fluid. Progressive daily increase of weight of 500 g or more should suggest the possibility of fluid retention. Pitting on pressure may

Table 15.3: Somatic abnormalities and congenital cardiac defects

Condition	*Chromosomal/ Genetic defect*	*Cardiac defects*	*Associated abnormalities*
Down syndrome	Trisomy 21	AV canal defects, VSD, ASD	Epicanthal fold, upslanted eyes, flat face, brachy cephaly
Turner's syndrome	45XO-Monosomy	Bicuspid aortic valve, Coarctation	Short stature, low ears, nuchal skin excess, wide set nipples
William's syndrome	Deletion 7q 11.23	Supravalvular AS	Mental retardation, face and teeth abnormalities
Holt Oram syndrome	Mutations on gene 12q24	ASD, VSD	Hand abnormalities especially of the radius, phocomelia
Ellis Van Creveld syndrome	Mutations on gene 4p16.1	ASD,Common atrium	Short limbs, short ribs,polydactyly, dysplastic nails, teeth
Noonan syndrome	Mutations in gene 12q22	PS, HCM	Mental retardation, facial dysmorpism
Leopard syndrome	Mutations in gene 12q22	PS, HCM	Lentigens, ocular hypertelorism abnormal genitals, retarded growth, deafness
Long QT syndrome	Autosomal dominant/ recessive	Long QT interval, sudden cardiac death (SCD)	With or without deafness
Brugada syndrome	Mutations in SCN5A	ECG variation SCD	SCD, VT, Syncope

be demonstrable only after several liters of edema fluid have accumulated in the system.

Cyanosis and Clubbing

Central cyanosis occurs in cyanotic congenital heart diseases, such as tetralogy of Fallot, transposition of great vessels, truncus arteriosus, total anomalous pulmonary venous drainage, tricuspid atresia, pulmonary atresia, Ebstein's anomaly, double outlet ventricles etc. In most of them cyanosis is present at birth or develop a few months later.

Conditions where there is left to right shunt such as uncomplicated ventricular septal defect (VSD), atrial septal defect (ASD) and patent ductus arteriosus (PDA) are acyanotic for considerable periods of time, often up to 3 or 4 decades or more. With the development of secondary pulmonary hypertension the shunt reverses and entry of right sided blood into left side gives rise to cyanosis. This phenomenon is called Eisenmenger's syndrome.

Cyanotic spells are attacks of intense cyanosis accompanied by marked breathlessness and disappearance of cardiac murmurs. These occur commonly in tetralogy of Fallot. These are often precipitated by feeding, crying or exertion.

Central cyanosis gives rise to secondary polycythemia and the increased viscosity of blood predisposes to thrombotic accidents, especially in cerebral veins.

Clubbing of the fingers and toes is of severe degree (grade 4) in cyanotic congenital heart disease. Clubbing is also a feature of infective endocarditis. In infective endocarditis clubbing may develop over normal nails within weeks or months and these are of lower grades. They are painful. Painful clubbing may also be a feature of hypertrophic osteoarthopathy, associated often with malignant lesions such as bronchogenic carcinoma and this has to be borne in mind. Splinter hemorrhages may develop under the distal third of the nails (Refer Fig. 2.21). Osler's nodes are painful red macules over the palms and soles. Janeway lesions are small painless macules, a few mm in diameter found on the palms and soles. Roth's spots are seen in the retina.

Temperature of the Extremities and Color

When the arterial circulation is adequate the extremities are warm and normal in colour. Presence of warm extremities point to normal cardiac output or high output states. Vasoconstriction leads to pallor. Coldness of extremities points to reduction in the arterial blood flow. In low output states the extremities are cold.

Extreme coldness of one limb or a part should suggest the occurrence of arterial occlusion.

Edema

Peripheral edema occurs in right sided heart failure. Look for pitting edema by pressure below the medial malleoli in ambulant subjects and over the sacrum in bedridden patients (Refer Figs 2.28A and B).

Pulmonary edema is a complication of left sided heart failure. Pulmonary edema leds to cough and dyspnea. Auscultation reveals persistent crepitations over the dependent regions of the lung. The sputum is watery and may show fresh blood streaking.

Temperature

Infective endocarditis, rheumatic fever, pericarditis, embolic episodes and atrial myxomas may present with fever. Several systemic infections such as typhoid, and influenza may produce cardiac complications. Even if the heart is not primarily affected, rise of temperature leads to tachycardia. This factor has to be taken into consideration before assessing the significance of tachycardia.

Respiratory rate

This is increased in dyspneic subjects. Tachypnea and dyspnea are common accompaniments of left sided heart failure.

General Decubitus of the Patient

Patients with left sided heart failure prefer to adopt a propped posture with head raised on several pillows. Orthopneic patients get relief on sitting up and leaning forwards over a cardiac table.

Mental State

Mental confusion and stupor may signify severe anoxic states or very low cardiac output.

Xanthomas/Xanthelasma

These are nodular masses which may be seen as subcutaneous tumors (xanthoma tuberosum), around tendons (xanthoma tendinosum), as plaques (xanthoma planum) These contain macrophages laden with cholesteryl esters. They suggest the possibility of familial hypercholesterolemia. Such persons have a great predilection to develop precocious ischemic heart disease. Xanthelasma palpebrarum occurring over the eyelids or below eyes is a common finding but has no direct relation to ischemic heart disease.

EXAMINATION OF PULSE

Pulse represents the expansile impulse produced by ventricular ejection and transmitted along the arteries. Examination of the pulse is a very important and rewarding method in the diagnosis of cardiovascular disease. This art should be practised by all students of medicine meticulously. In Ayurveda, examination of the pulse "Naadi" has been described in great detail.

Method of Palpation of Pulse

Ordinarily, the radial pulse is examined by palpation above the wrist (Fig. 15.1). Other arteries which also must be palpated include brachial arteries in the cubital fossae, carotid arteries in the neck, femoral arteries in the groins, popliteal arteries in the popliteal fossae, dorsalis pedis over the dorsum of foot, and posterior tibial behind the medial malleolus. Absence of pulse in any of these locations may be due to either proximal occlusion of arteries or an aberrant course of the artery. Reduction in amplitude of pulses may be due to partial obstruction of the artery in many cases. In a few, it may occur without disease. Weak pulse may be felt distally over an artery, even in the presence of proximal occlusion, if collateral circulation develops (Figs 15.1 to 15.3).

While examining the pulse the following points are specifically noted, viz the pulse rate, rhythm, volume, character, equality on both sides, radiofemoral delay, state of arterial walls and other peripheral pulsations (*see* Figs 15.1 to 15.3).

Pulse Rate

Count the pulse for 1 minute. Normal pulse rate at rest varies from 60 to 100 per minute. Tachycardia is heart rate above 100 per minute and bradycardia is heart rate below 60 per minute.

The pulse is often below 40 per minute in myxedema, heart blocks and toxicity caused by drugs like digitalis or poisons like *Cerbera odollam.* Raised intracranial tension and obstructive jaundice leads to bradycardia. In heart block, the pulse does



Fig. 15.1: Palpation of radial pulse



Fig. 15.2: Palpation of femoral pulse



Fig. 15.3: Palpation of popliteal artery

not increase with exertion, whereas it does so in sinus bradycardia. In atheletes and persons doing heavy work the resting pulse rate is slow due to vagotonia. It promptly increases with exercise.

Marked tachycardia should suggest cardiac disorders such as heart failure, paroxysmal tachycardias and myocarditis. General conditions which give rise to tachycardia are fever, thyrotoxicosis, tuberculosis, and the use of sympathomimetic drugs.

Look for *pulse deficit*, i.e. difference between heart rate and pulse rate by simultaneous auscultation of the heart and palpation of the pulse by 2 persons.

Rhythm of the Pulse

The rhythm of pulse denotes the regularity with which each beat succeeds another. Normally the pulse is regular on palpation. Even in health it can be slightly irregular, e.g. sinus arrhythmia. Sinus arrhythmia is the acceleration of pulse during inspiration and slowing during expiration. This is caused by alterations in vagal tone. *Sinus arrhythmia* is more obvious in children and young adults. Very often, irregularity in pulse is a sign of disease.

Abnormal Rhythms

The pulse may be irregular in several disease states. *Extrasystoles or ectopics* are premature beats originating from sites other than the SA node. Depending on their site of origin, they may be termed ventricular or supraventricular. Many ectopic beats block or interfere with the subsequent normal beat and a pause results. This is referred to as the compensatory pause, which is the hallmark of ectopic beats. Generally ectopic beats disappear when the heart rate increases as a result of exercise. A run of ectopic beats due to enhanced automaticity is a mechanism for paroxysmal tachycardias. Their rate depends on the specific type of paroxysmal tachycardia.

Another common arrhythmia is *atrial fibrillation.* The pulse is irregularly irregular in this condition. There is irregularity in rhythm and the volume of the pulse. The irregularity often increases with exertion.

Atrial flutter is less common. In this arrhythmia, atria contract regularly at rates ranging from 250 to 300 per minute. The ventricles contract at a much slower rate due to associated A-V block. The ventricular rhythm maybe regular or irregular depending on the nature of the coexisting A-V block.

In *heart blocks* the pulse is regularly irregular. However, if the block tends to vary from time-to-time, the pulse may also become irregularly irregular. Usually the irregularity does not change with exertion. Though a preliminary idea can be obtained by palpation, for all practical purposes, ECG recording is mandatory for final diagnosis.

Pulsus Bigeminus

This is the occurrence of two beats in succession, followed by a compensatory pause. This commonly occurs when every normal beat is followed by an extrasystole. This is characteristically seen in digitalis toxicity. Other causes for a bigeminal rhythm include 3:2 conduction blocks at any site and also escape capture bigeminal rhythm.

Volume of the Pulse

This denotes the amplitude of movement of the vessel wall due to the passage of the pulse wave. It correlates with stroke volume of the heart. In high cardiac output states the amplitude is increased, e.g. aortic incompetence and mitral incompetence. Amplitude of pulse is less (pulsus parvus) in low cardiac output states such as mitral stenosis or aortic stenosis with cardiac failure. In shock, the pulse is rapid and feeble (thready pulse).

Character of the Pulse

Normal pulse can be graphically represented as given in Figure 15.4. It has an anacrotic wave consisting of the percussion wave and the tidal wave. The pulse tracing also shows small notch on the descending limb, known as the dicrotic notch, followed by the dicrotic wave. The beginner may find it difficult to identify the tidal wave and dicrotic notch by palpation, but when these become exaggerated in disease states, they are palpable easily. The total duration of the radial pulse is 300 msec. when the heart rate is around 70 to 80 per minute.

Abnormalities in the Character of the Pulse

Dicrotic pulse: The dicrotic wave becomes more prominent and can be felt as a "notch" in the descending limb. This is an exaggeration of the normal pattern and it is not suggestive of any cardiovascular disease. This is seen in fevers, e.g. typhoid, due to reduction in vascular tone.

Anacrotic pulse: This is a slow rising pulse of smaller amplitude and delayed peak—pulsus parvus et tardus seen in conditions like aortic stenosis. Due to delay in ejection and reduction in the pressure in the aorta, the pulse is smaller in amplitude and is wider.

Bisferiens pulse: The pulse form shows two positive peaks during systole. After the initial rapid forceful upstroke, a second smaller peak is also felt (Fig. 15.4). The former is the percussion wave and the latter is the tidal wave.

This is seen typically in combined aortic stenosis and incompetence. It can also occur in pure aortic incompetence and hypertrophic obstructive cardiomyopathy. Bisferiens pulse is best palpable over the major arteries such as common carotid, brachial or femoral, though the experienced hand can identify this pattern over all arteries.

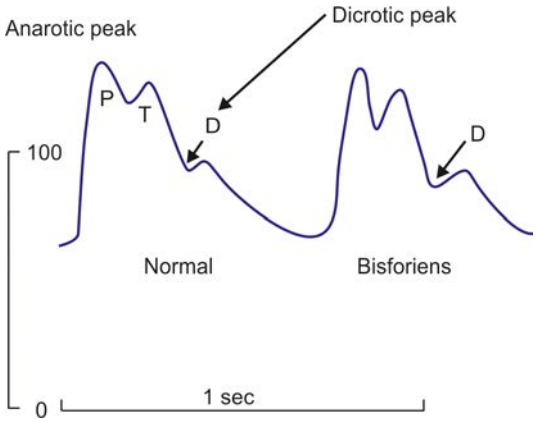


Fig. 15.4: Pulsus bisferiens. (P–percussion wave, T–tidal wave, D–dicrotic notch)

Collapsing pulse (Syn: Corrigan's pulse, waterhammer pulse): This is seen in conditions where the stroke volume is high and the peripheral resistance is low, classically occurring in free aortic incompetence.

Method: Palpate both the radial and ulnar arteries with the palm, above the wrist. Then elevate the hands above the level of the patient's head. In normal individuals only the radial artery is distinctly felt and there is no appreciable difference when the hand is elevated (Fig. 15.5).



Fig. 15.5: Method to palpate collapsing pulse, both radial and ulnar arteries are felt by the examiner's palm

In aortic incompetence, both the pulses become more prominent and they collapse suddenly. The feeling is that of air bubbles entering a bottle filled with water, which is inverted to empty the contents. This phenomenon is comparable to the effect produced by a waterhammer—which is a toy popular in the west.

Other conditions in which collapsing pulse occurs are patent ductus arteriosus and rupture of the aneurysm of sinus of Valsalva. The term "pseudocollapsing pulse" is used to denote a high volume pulse which also drops abruptly, as is seen in mitral incompetence.

Pulsus paradoxus: Normally when the pulse is palpated with the patient breathing normally a slight reduction in the amplitude of the pulse occurs during inspiration. Often this is imperceptible. Marked reduction in amplitude occurs in constrictive pericarditis, pericardial effusion and cardiac tamponade. This exaggeration of the normal fluctuation is termed pulsus paradoxus and is defined as a pulse in which the systolic BP falls by more than 10 mm Hg during quiet inspiration.

Pulsus alternans: This is the phenomenon in which every alternate pulse is weak. This phenomenon can be objectively confirmed by recording the blood pressure. While recording the blood pressure, when the initial systolic blood pressure is recorded only the stronger beats are transmitted. When the mercury column is further lowered, there is an abrupt doubling of Korotkoffs sounds, at which stage all the beats are transmitted to the pulse. It will be seen that the difference in systolic blood pressure between alternate beats may be even as high as 40 mm Hg. Pulsus alternans is often a feature of left ventricular failure.

Detection of Pulse Delay

The two radial pulses come synchronously. When the radial pulse and ipsilateral femoral pulse are palpated simultaneously, the femoral pulse is felt a bit before the radial pulse (5 msec). Delay in the femoral pulse suggests obstruction to the aorta as is seen in coarctation (Fig. 15.6).

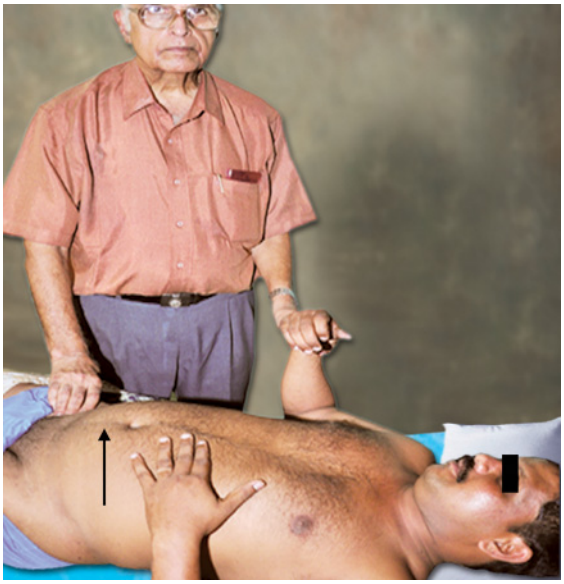


Fig. 15.6: Detecting radiofemoral delay. Femoral artery is palpated with the right hand while examining the radial pulse

Arterial Wall Thickness

This is done to assess the state of the medium sized arteries which are palpable.

Method

Palpate the radial artery with the middle three fingers. Occlude the artery proximally and using the distal finger empty the artery by pressing out the blood peripherally. While applying pressure on either side to keep the arterial segment empty the middle finger rolls the artery over the underlying bone to assess its thickness and consistency.

Normally, the artery is just palpable as a soft collapsible tube. Thickening, irregularity and cord-like feel suggest arteriosclerosis which affects the medium sized *arteries—Monckeberg's sclerosis*. This is a change occurring with age, but in some cases it is more pronounced. The main abnormality is in the medial coat of the arteries and this change does not reflect atherosclerosis. Atherosclerosis takes place in the intima and is associated with occlusive arterial disease.

Auscultation over Arteries

Before concluding the examination of the arteries, some of the major arteries should be auscultated to elicit diagnostic findings. These include the carotid, vertebral and femoral arteries, abdominal aorta, renal arteries and iliac arteries.

Normal blood flow through the arteries does not give rise to bruit. Bruit occurs when there is

increased blood flow through normal arteries or normal or reduced blood flow through narrowed and roughened arterial lumen. Auscultation is helpful to assess the state of blood flow in arteries if abnormalities are detectable.

Method

The stethoscope is applied with sufficient pressure to reach the artery, taking care not to compress it, and the events are noted.

Bruits in the neck may be detected in a small proportion of apparently normal persons without disease.

Pistol shot sounds: These are sharp sounds heard over major arteries like the femorals and brachials in the presence of aortic regurgitation.

While auscultating over the femoral artery, apply pressure on the artery proximal to the chest piece of the stethoscope. A systolic murmur develops. Apply pressure distally, and a diastolic murmur develops.

Duroziez murmurs: These are murmurs that can be heard over the femoral arteries in free aortic incompetence.

Note: Routine auscultation over arteries can be done along with auscultation of the heart, especially so in cases where abnormalities are expected.

Clinical Significance of Examination of the Pulse

Important parameters of cardiac function such as the rhythm, force of contraction, cardiac output and hemodynamic abnormalities and the state of the vascular bed can be reliably assessed by careful examination of the pulse.

EXAMINATION OF THE JUGULAR VEINS

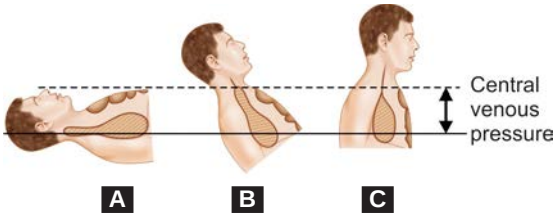
Examination of the jugular vein gives important information about hemodynamics of the right side of the heart. The internal jugular vein on the right side is preferred, because the pressure changes in the right atrium are transmitted directly through the superior vena cava and innominate vein, without interposition of valves.

Method

The patient should be lying comfortably at an angle of 45° incline, with clothing removed from the neck and upper thorax. The head and thorax should be in line, without kinking.

45° incline is selected due to the following reasons: In supine position, the internal jugular veins are full even in normal persons. At 45° incline the sternal angle (angle of Louis) and the sterno-clavicular joint are at the same level. Therefore, the top of blood column in the internal jugular vein can be measured from the sternal angle as shown in (Figs 15.7 and 15.8).

The center of the right atrium is 5 cm below and behind the sternal angle. Normal right atrial pressure is 5 to 7 cm of blood column and at this level the top of blood column is seen just behind the right sternoclavicular joint. Any rise in right atrial pressure will be reflected as elevation of blood column in the jugular vein. The jugular venous pulse is best seen when a light is held tangentially over the neck. In most of the patients, 45° incline is



Figs 15.7 A to C: Height of jugular venous coloum in different positions of the patient: (A) supine, (B) 45º incline, (C) sitting up

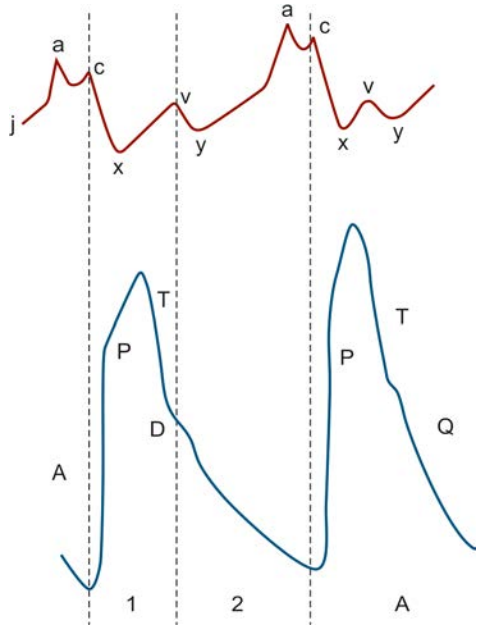


Fig. 15.8: Normal tracing of jugular vein and carotid artery. Jugular venous pressure tracing— waves a,c and v and troughs x and y are seen, and A—arterial pulse, P— percussion wave, T—tidal wave, D—dicrotic notch, 1—systole, 2—diastole

adequate to identify the upper level of jugular venous column, but if the venous pressure is unusually high, the angle of incline should be reduced and some patients may have to be examined even sitting up.

Sometimes difficulties may be experienced in differentiating the carotid arterial pulsation from the jugular venous pulse. The points of distinction are given in Table 15.4.

Examine the JVP to elicit the following information:

1. Height of venous column, expressed as the vertical height above the level of sternal angle.
2. Venous pulsations.
3. Hepatojugular reflux (abdominojugular reflux).

The jugular venous pulse has 3 positive waves, a, c and v and 2 negative waves x and y. The "a" wave is caused by atrial systole. The "c" wave is due to bulging of the A-V valve apparatus into the atrium during the onset of ventricular systole. The "v" wave is due to venous inflow and rise in pressure in the atria during ventricular systole. The "x" descent is due to atrial relaxation and also due to the ventricular contraction pulling down the floor of the atrium towards the ventricular aspect. The "y" descent is due to rapid atrial emptying in the early part of ventricular diastole. The waves in the jugular vein are identified by timing with the carotid pulse. "a" wave occurs just before the carotid pulse whereas the "v" wave coincides with it (Figs 15.8 and 15.10).

Table 15.4: Points of distinction between carotid artery pulsation and jugular venous pulse

Pulsation	*Jugular venous*	*Carotid artery pulsation*
1. Site	Behind the sterno-mastoid muscle	Deep to sternom-astoid
2. Form	Wavy, three positive wave	Jerky, only one systolic wave
3. Timing	Occurs throughout the cardiac cycle	Only during systole
4. Influence of position	Becomes more prominent when patients lies flat	No change with position
5. Change during phases of respiration.	During inspiration vein empties and vice versa	No change
6. Hepatojugular reflux	Venous column becomes more prominent	No change
7. Palpability	Easily occluded non-palpable	Well palpable

The abdominojugular reflux is tested by applying firm pressure over the upper abdomen for 10 to 30 seconds with the patient breathing normally. In a normal subject the jugular venous pressure rises transiently and falls to normal even when the pressure is continued. In presence of cardiac failure the elevation of the jugular venous pressure is prominent and sustained. Positive abdominojugular reflux also indicates that the inferior and superior vena cava are patent (Fig. 15.9).

Alteration in Diseases

Jugular venous pressure (JVP): Elevation of the jugular venous pressure reflects increase in right atrial pressure and this occurs commonly in right heart failure. Other less common causes include the reduction in compliance of right ventricle as is seen in severe right ventricular hypertrophy, pericardial diseases, and right ventricular



Fig. 15.9: Eliciting hepatojugular reflux. Apply gentle, but firm pressure continuously over the right hypochondrium. Look for engorgement of the jugular vein in the neck in the position of the arrow

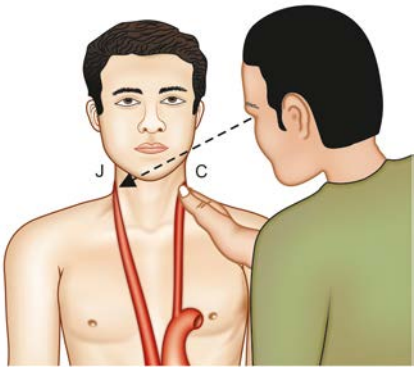


Fig. 15.10: Examination of upper limit of jugular venous column: J–Simultaneous palpation of the opposite carotid artery helps to determine timings of the jugular waves, C–carotid artery

endomyocardial fibrosis. Tricuspid valve disease also causes a raised JVP. In superior venacaval obstruction the jugular veins are engorged and nonpulsatile. Conditions of increased blood volume like pregnancy and acute glomerulonephritis are associated with raised JVP.

Normally during inspiration the JVP falls. A paradoxic inspiratory rise in the height of the jugular venous column is known as *Kussmaul's sign.* This is seen in constrictive pericarditis, pericardial effusion, cardiac tamponade, congestive cardiac failure and tricuspid stenosis.

Alterations in the Pattern of Jugular Venous Pulsation

Giant "a" waves: The "a" wave is particularly prominent in conditions where the right atrium contracts with greater force as in atrial outflow obstruction, e.g. tricuspid stenosis, or where the right ventricular compliance is diminished as in hypertrophy or infarction. When the "a" waves are prominent and clearly visible, they are called *giant "a" waves.*

Cannon waves: Cannon waves occur when the atrium contracts against a closed tricuspid valve due to AV dissociation. Irregular and random cannon waves occur in atrioventricular dissociation, e.g. complete heart block, ventricular ectopics and ventricular tachycardia. In nodal rhythm, i.e. impulse originating from the A-V node, regular cannon waves occur.

Though cannon waves are of atrial origin, they are systolic events and coincide with the carotid pulse in timing, unlike giant 'a' waves which are presystolic. Often the force of the atrial contraction in cannon waves is so large as to reach up to the angle of the jaw.

Absence of "a" waves: In atrial fibrillation, since the atrium does not contract as a whole, the "a" waves disappear. This is an important diagnostic sign of atrial fibrillation.

V waves: In tricuspid incompetence the "v" wave becomes prominent. In atrial fibrillation also the "v" wave is prominent. Identification of the abnormalities of the positive waves is easier than those of the negative waves. Still, with experience, several abnormalities of the negative waves can be recognized and these are of diagnostic importance.

"X" descent: This is prominent in cardiac tamponade, and it disappears in atrial fibrillation. "y" descent This is prominent (sharp and deep) in constrictive pericarditis and tricuspid regurgitation. It is sharp, but not deep in restrictive cardiomyopathy. "y" descent is shallow and gradual in tricuspid stenosis in which atrial emptying is delayed.

EXAMINATION OF THE CHEST—DILATED VEINS ON THE CHEST

These are seen in vena caval obstruction. In obstruction to superior vena cava caused by mediastinal obstruction, dilated and tortuous veins may be seen over the neck and upper part of chest, with blood flow directed towards the abdomen. It is rare for cardiovascular lesions to produce mediastinal obstruction, but it may occur in aneurysm of the arch of the aorta. In inferior vena caval obstruction dilated veins from the upper abdomen are seen to pass up the chest to drain blood into the area of drainage of the superior vena cava. Localized venous engorgement may denote underlying inflammation (e.g. empyema) or neoplasm (e.g. pleural malignancy).

Shape of the precordium: Precordium is that portion of the chest wall which overlies the heart. Inspect the precordium and the chest as a whole for abnormalities of shape.

Precordial bulge occurs in congenital heart disease associated with enlargement of the right ventricle, e.g. large atrial septal defect, severe pulmonary stenosis. Similarly gross pericardial effusion and endomyocardial fibrosis occurring in childhood may also give rise to precordial bulge. Aortic aneurysms may erode anteriorly on to the chest wall, and may be seen and felt as localized bulges, often pulsatile.

Primary abnormalities of the thoracic cage may give rise to displacement of the heart and abnormal cardiac findings. In severe *pectus excavatum* the heart is displaced posteriorly and to the side. In kyphoscoliosis the heart is displaced towards the convex side. In persons with straight back syndrome the heart may be displaced to either side or compressed anteroposteriorly.

Pulsations on the Chest Wall

Examine the patient in the supine or 45° incline position. Look for the following pulsations.

Apex beat: In the majority of normal persons the impulse produced by the apex of the left ventricle which impinges on the chest wall is seen as a localized pulsation in the fifth left intercostal space. For convenience the apex beat is described in relation to the left midclavicular line. The apex beat is 1 to 1.5 cm medial to it. Apex beat is better seen and felt when the breath is held in expiration. In obese subjects with normal hearts the apex beat may not be visible. In emphysema and pericardial effusion, the apex beat is not visible and if at all palpable, it may be faint. Displacement of the apex may occur in several conditions. If the apex beat is not readily visible inspection from the side with tangential lighting may reveal the pulsation.

Cardiomegaly: When the heart enlarges, the apex beat is displaced laterally. Position of apex beat should be examined when the patient is lying supine and maybe fallacious if left lateral position is assumed. However feeling the apex beat in the left lateral position may help in assessing the character of apex beat or other palpable events over the apex beat. In right ventricular enlargement the displacement is more horizontally outwards, whereas in left ventricular enlargement the displacement is both downwards and outwards. In extreme cases the apex beat may be seen as low as the seventh left intercostal space and as far out as the midaxillary line or even beyond.

Displacement of the heart: Conditions which encroach upon the volume of the thoracic cavity and diseases affecting the pleural cavities and lungs lead to displacement of mediastinal structures. In pleural effusion and pneumothorax, the heart is pushed to the opposite side. In collapse and fibrosis of the lungs, the heart is pulled towards the side of lesion.

Dextrocardia is a developmental anomaly in which the heart occupies the right hemithorax and the apex beat is seen on the right fifth intercostal space. This anomaly resulting from the malrotation of the heart during embryogenesis may occur in several forms.

When dextrocardia is associated with corresponding anomalous position of the abdominal and other thoracic viscera it is called *"dextrocardia with situs inversus totalis"*, i.e. heart is on the right side and liver is on the left. In this combination, the heart *per se* often does not show any serious anatomical or functional abnormalities. However when the heart alone is on the right side and all other viscera are in their normal positions, i.e. isolated dextrocardia with "situs solitus", the chances for major anatomical and functional cardiac defects are great.

Precordial Pulsation

In normal adults with moderate build the precordium does not pulsate visibly as a whole, except during physiological increases in cardiac output caused by exertion or emotional stress. Presence of prominent precordial pulsations at rest should suggest the presence of ventricular enlargement or aortic aneurysm. Since the right ventricle occupies the diaphragmatic surface and medial part of the anterior surface of the heart, enlargement of the right ventricle gives rise to left parasternal pulsations. In gross enlargement of the right ventricle, as in atrial septal defects or mitral stenosis the right ventricle may occupy almost the whole of the anterior surface and the pulsations may be more widespread.

Left ventricular enlargement associated with increased stroke volume, as is seen in aortic incompetence leads to visible precordial pulsations occupying part or whole of the precordium.

Another rare cause of precordial pulsations is aortic aneurysm. Aneurysm of ascending aorta causes expansile pulsation to the right of the sternum better felt with the patient sitting up and holding the breath in expiration. Aneurysm of the arch of the aorta erodes the upper part of sternum and may present as a localized bulge. Widening of upper mediastinum can be made out by percussion. Aneurysm of the descending thoracic aorta is usually silent, but expansile pulsation felt at the back on the side of the vertebrae may offer telltale evidence. Aneurysm of abdominal aorta can be easily seen and palpated per abdomen.

Epigastric Pulsation

The epigastrium shows only faint pulsations when a normal adult rests in the supine or 45° incline position. This pulsation is transmitted from the right ventricle across the diaphragm and left lobe of the liver. In children, thin subjects and in tachycardia, more prominent epigastric pulsation may be seen even in the absence of disease.



Fig. 15.11: Palpation of the epigastrium for right ventricular pulsations



Fig. 15.12: Palpation of expansile palpation of the liver

Epigastric pulsations should be considered pathological when they are unduly prominent, sustained, and they occur even with slow heart rate.

Causes of Abnormal Epigastric Pulsations

1. *Right ventricular enlargement:* For example, atrial septal defect, mitral stenosis. Since right ventricular stroke volume increases during inspiration, the pulsations also increase correspondingly. Right ventricular impulse is better felt on the tip of the fingers in contrast to the liver or aortic pulsations which are better felt on the pulp of the fingers (Fig. 15.11).
2. *Expansile pulsations of the liver:* In tricuspid incompetence the liver shows systolic pulsations which increase with inspiration. Right atrial pressure changes are transmitted directly to the liver through the inferior vena cava and hepatic veins which are all in direct communication with the right atrium (Fig. 15.12).
3. *Aneurysm of abdominal aorta:* Large abdominal aneurysms of the aorta may reach the surface and give rise to expansile systolic pulsations in the epigastrium and umbilical region in the midline.

Transmitted pulsations from normal aorta: When solid masses such as tumors or enlarged lymph nodes interpose between the aorta and the anterior abdominal wall, aortic pulsations will be visible in the epigastrium. This pulsation is not expansible. Even in very thin normal subjects aortic pulsation can be seen and felt. This is not pathological.

Significance of epigastric pulsation: This is a reliable and easily detectable sign of right ventricular enlargement, if the other causes can be excluded.

Pulsation of the great vessels: Pulsations arising from the pulmonary artery and aorta are visible over the left and right second and third intercostal spaces respectively.

PALPATION OF THE PRECORDIUM

Technique of Palpation

The chest and abdomen are exposed from the sternoclavicular joint above to the umbilicus below. The patient lies supine comfortably or at an angle of 45° in bed. The examiner should sit on the right side and palpate the apex beat with the palm of the hand and finger tips. Later, with the ulnar border of the hand palpate for left parasternal heave. If the apex beat is not clearly palpable, the patient is made to turn to the left lateral position with the examiner's palm held firmly over the precordium, more laterally. Usually in this position the apex beat shifts outside by 2 to 3 cm and becomes more palpable. Events occurring at the mitral valve such as mitral diastolic murmurs and the loud and snapping first heart sound are better appreciated in the left lateral position, with breath held in expiration. If the apex beat is not felt



Fig. 15.13: Locating the apex beat with tip of the fingers of the right hand. The left hand palpates the intercostal spaces

in the usual position, it should be looked for in other positions as far as the back of the chest, to detect displacement. Particularly palpate on the right side, so that dextrocardia is not missed. Having identified the apex beat, localization and description of the apex beat should be done in the supine position or at 45° incline. All the palpatory abnormalities which indicate structural and functional changes in the heart are related to the findings obtained in this position (Fig. 15.13).

Look for:

1. The apex beat—position and character.
2. Palpable sounds
3. Presence of thrills
4. Precordial pulsation
5. Left parasternal heave
6. Right parasternal pulsations
7. Pulsations in the second and third intercostal spaces which arise from the pulmonary artery on the left side and ascending aorta on the right.

Having completed the palpation in the lying position, if the condition of the patient permits, palpation should be done with the patient sitting up and leaning forward. Since the mediastinal structures come closer to the palpating hand in this position, pulsations of the great arteries, events arising from the semilunar valves and thrills arising from them are felt better in the sitting up position.

Observing the Changes with Respiration

The changes occurring during inspiration and expiration should be observed. Events arising from the right side of the heart such as tricuspid valve murmurs, right ventricular pulsation and pulmonary artery murmurs increase during inspiration, on account of the transient increase in blood flow through the right side. Left sided events such as mitral murmurs, and aortic murmurs increase during expiration, since blood flow through the left side increases during expiration. Moreover, since the lungs recede from the precordium, events arising from the left side are transmitted better to the chest wall during expiration.

Apex Beat

It is the outermost and lowermost position on the chest wall where a distinct lift caused by cardiac contraction is felt. This is often appreciated by the palm of the hand, but exact localization may require palpation by the finger tips. In obese individuals and those with thick chest wall, the apex beat may not be easily identifiable. When the apex beat is behind a rib it may not be readily felt. In a small proportion of normal individuals the apex beat may not be palpable. In them other methods have to be employed to assess the cardiac size. Once the apex beat is located look for the following points:

1. Position
2. Character.

In normal persons the apex beat is felt at the fifth left intercostal space 1 to 2 cm inside the left mid clavicular line. It can be distinctly felt and it just lifts the palpating finger. In children and thin subjects it is felt better. The apex beat is produced by the contraction of left ventricle in the vast majority of cases.

When right ventricular enlargement is gross, it may occupy the position of the apex and the impulse may arise from this ventricle. This is rare.

Position

Shift of apex may be due to enlargement of the heart (cardiomegaly) or displacement. The approximate size of the heart can be determined by percussing its right and left borders. When the heart is enlarged the right border remains at the normal position or is enlarged to the right side, whereas the left border is displaced outwards (Fig. 15.14).

In displacement, the right border of the heart also shifts along with the apex.

Character

Abnormalities include *hyperdynamic apex beat, heaving apex beat, tapping apex beat, double impulse, and feeble apex beat.*



Fig. 15.14: Defining the position of the apex beat by counting the intercostal spaces (arrow) points to second left intercostal space just below the sternal angle

When the apex beat is more forceful and the amplitude of elevation of the palpating finger is beyond the plane of the adjoining ribs, it is called *hyperdynamic or forceful apex beat*. This signifies increase in left ventricular end diastolic volume and stroke volume. Forceful apex beat is seen in conditions such as aortic incompetence and mitral incompetence, where ejection occurs against normal or reduced resistance. In other words, these are conditions, where the preload of the ventricle is increased and ventricular enlargement is more prominent than muscle hypertrophy.

Heaving apex beat is one in which the strong apical impulse lifts the palpating finger beyond the plane of the adjoining ribs and this lift is sustained for more than half of the duration of systole. This signifies increased muscle mass occurring in ventricular hypertrophy. Most commonly these are seen in conditions where the ventricle has to eject blood against increased and sustained resistance such as aortic stenosis or arterial hypertension. In other words conditions which increase the after load give rise to muscle hypertrophy which is reflected as heaving apex beat.

Tapping apex beat is classically found in mitral stenosis. This term refers to the ill-sustained, but distinct impulse felt by the palpating hand comparable to a "tap at the door". It is associated with a loud first heart sound which is responsible for the alteration in quality of the apex beat.

Double impulse may be felt when there is dynamic obstruction to left ventricular ejection as is seen in hypertrophic obstructive cardiomyopathy, and when there is decreased left ventricular compliance as in hypertension, aortic valve diseases, coronary artery disease or left ventricular aneurysm. This second impulse may occur during systole or during late diastole (presystole).

The apex beat is pathologically feeble when ventricular contraction is weak as occurring in severe forms of cardiac failure, shock, hypovolemic states and extensive disease of the cardiac muscle. The apex beat may be feeble in pericardial effusion, constrictive pericarditis and emphysema since in these conditions left ventricular contraction is not directly transmitted to the chest wall. If palpation fails to locate the apex beat, the position of cardiac apex can be ascertained by auscultation. The point of maximum loudness of mitral events, especially first heart sound is taken to correspond to the left ventricular apex.

Left Parasternal Pulsations

The ulnar border of the hand is placed over the 3rd, 4th and 5th left intercostal spaces by the side of the sternum and the systolic elevation of the lower left costal cartilages is felt as the left parasternal impulse.

Palpable pulsation of the left parasternal region may be felt in thin individuals even normally, especially when there is tachycardia. Occurrence of prominent pulsations at rest may signify abnormalities of right ventricular function. It should be distinguished whether the prominent pulsation is only an increased amplitude of movement or whether both amplitude and duration of the pulsation are increased. The former is called a left parasternal lift and the latter is termed left parasternal heave (Fig.15.15).

Left parasternal pulsations are commonly caused by conditions associated with enlargement or hypertrophy of the right ventricle due to volume or pressure overload. Forceful left parasternal lift occurs in conditions such as atrial septal defect and tricuspid incompetence which cause volume overload. Sustained left parasternal heave indicates pressure overload and this occurs in pulmonary artery hypertension and pulmonary stenosis. The interpretation is similar to that described for the apex beat. Although commonly associated with right ventricular volume or pressure overload, a left parasternal impulse may also be felt in other conditions like ventricular aneurysms, aneurysms of the ascending or descending thoracic aorta and



Fig. 15.15: Palpating the left parasternal region for pulsations and heave

severe left atrial enlargement as in mitral regurgitation. The left parasternal impulse due to severe mitral regurgitation is classically a late systolic lift and is due to the dilated left atrium.

Pulsation of Great Vessels

Palpation over the second and third intercostal spaces with the pulp of the thumb or the palm reveals pulsations if there is dilatation of the aorta or pulmonary artery and increased flow through them. Pulmonary artery and pulmonary valve closure are felt on the left second intercostal space (Fig. 15.16). Aortic events are felt better on the right.



Fig. 15.16: Palpation of the second left intercostal space for pulsations, valve closure sound and thrills

Thrills

These are palpable murmurs. Loud murmurs (grade IV or more) are palpable as thrills. Increased flow across a normal valve or turbulent flow across diseased valves gives rise to murmurs. Congenital and acquired defects which lead to abnormal blood flow also give rise to thrills.

Thrills arising from the mitral valve are mostly diastolic. The mid-diastolic murmur with presystolic accentuation occurring in mitral stenosis is felt as a thrill, comparable to the purring of a cat. Systolic thrill over the mitral area indicates mitral incompetence (Fig. 15.17). From the tricuspid valve systolic murmurs and diastolic murmurs give rise to thrills, the former being more common. They indicate tricuspid incompetence and stenosis respectively. Tricuspid events accentuate during inspiration.

From the pulmonary and aortic valves, systolic thrills produced by stenotic lesions are easily felt. Pulmonary thrills are felt over the pulmonary area, i.e. second left intercostal space close to the sternum. These increase with inspiration. Aortic systolic thrills are felt over the aortic area, i.e. second right intercostal space close to the sternum. They are best felt with the patient sitting up and holding the breath in expiration. Diastolic murmurs arising from the aortic and pulmonary valves produce thrills less



Fig. 15.17: Palpation over apex beats with patient in the left lateral position to detect particularly mitral diastolic thrill in mitral stenosis



Fig. 15.18: Palpation over third and fourth intercostal space for systolic thrills



Fig. 15.19: Palpation for aortic and pulmonary thrills
Note: Patient holds his breath in expiration

commonly. Continuous thrill may occur, occupying both systole and diastole when the murmurs are continuous as in *patent ductus arteriosus* (PDA) or rupture of the *aneurysm of the sinus of valsalva*. Rarely in aortic stenosis with incompetence, systolodiastolic thrills may be obtained. These are not continuous, but show a gap in-between.

Palpation over the third and fourth left intercostal spaces may bring out the systolic thrill of ventricular septal defect (Figs 15.18 and 15.19).

In coarctation of the aorta, collateral arterial circulation may develop over the chest. The intercostal arteries become prominent and pulsatile and thrills may be felt widely over the scapular margins and thoracic cage.

Palpable Heart Sounds

When the third and fourth heart sounds are loud, they may become palpable.

Extracardiac Events

Pericardial rub can be palpated as a leathery rub more commonly towards the upper part of the precordium, especially if the patient sits up and leans forward.

Pleuropericardial rub may be felt over the precordium during the phase of inspiration and when the breath is held in inspiration. During expiration the rub may diminish or disappear.

PERCUSSION OF THE PRECORDIUM

The general principles of percussion are the same as described alongwith the respiratory system. The precordium is less resonant than the rest of the chest, since the left lung does not fully cover the precordium under normal conditions. By gentle percussion, the transition from resonance to dullness can be made out and the heart borders percussed out. Though this method is less sensitive to define the exact size of the heart, it does give an idea of cardiac size and shape in the majority of cases, where the thoracic cage and lungs are normal.

Procedure

Start to mark out the upper border of the liver by percussing the right side of the chest from above downwards till it is reached. Liver dullness is defined first in order to make sure that the dullness produced over the right sternal region is not caused by an enlarged liver and also to confirm that the liver is on the right side.

The right border of the heart is defined by percussing from the right midclavicular line towards the sternum, keeping the plexiметer finger parallel to the sternal edge in the third and fourth intercostal spaces till the cardiac dullness is obtained. Normally the right cardiac border coincides with the right sternal border.

The left border is obtained by starting percussion from the left midaxillary line and proceeding towards the left border of the sternum. The plexiметer finger is kept vertically in the fourth and fifth left intercostal spaces. Generally the left border of the heart is 1 cm medial to the left midclavicular line and it corresponds to the apex beat. In pericardial effusion the percussed out cardiac dullness extends beyond the palpated apex beat.



Fig. 15.20: Percussing the upper border of the liver to confirm its position, before percussing the right border



Fig. 15.21: Percussing the right border of the heart in the direction shown by the arrow



Fig. 15.22: Percussing the left border of the heart in the direction of the arrow

The borders of the great arteries can be made out by percussing in the second left and right intercostal spaces, starting from the midclavicular lines and moving medially. Normally they do not extend more than 2.5 cm outside the sternal border. Enlargement of the pulmonary artery causes dullness towards the left and that of the aorta to the right (Fig. 15.23).

The lower border is closely apposed to the diaphragm and left lobe of the liver, and it cannot be percussed out separately. The cardiac borders are formed by the following structures (Figs 15.20 to 15.22).

Right border—right atrium

Left border—left ventricle, left atrial appendage, main pulmonary artery and aortic arch from below upwards.

The anterior surface is formed by the right ventricle medially, and the left ventricle laterally. The left atrium occupies the posterior surface of the heart and it is in close relation to the esophagus behind. The diaphragmatic surface of the heart is formed by the right ventricle.

Clinical Importance of Percussion

Percussion enables to define the cardiac borders approximately. To define cardiac size more accurately investigations like radiography and ultrasonography are required. In emphysema and left sided pneumothorax cardiac dullness may be obliterated. In left sided pleural effusion the whole of the left hemithorax is dull and heart borders cannot be distinguished.

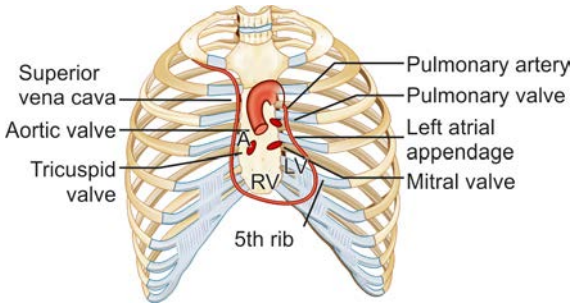


Fig. 15.23: Diagram showing the position of cardiac valves

Percussion helps to distinguish between cardiomegaly and cardiac displacement. In pericardial effusion, the left border extending beyond the apex beat is very suggestive clinical sign. Percussion is also useful for the detection or aortic aneurysms, pulmonary artery enlargement, right atrial enlargement and ventricular aneurysms.

Note: Wherever more reliable methods to assess cardiac size such as chest X-ray and echocardiography are freely available, they should be employed. When these facilities are not available, percussion has to be relied upon, though it is not a sensitive method.

AUSCULTATION OF THE HEART AND BLOOD VESSELS

Sounds which are produced by closure of heart valves, movement of the myocardium and great vessels, flow of blood into the ventricles and across normal and abnormal valves can all be auscultated using the stethoscope, which has assumed so much importance in clinical practice, so as to form the insignia of the doctor.

Several types and makes of stethoscopes are available. Some general principles may be borne in mind when choosing a stethoscope. Most of the models are suitable for ordinary work and it is the experience obtained by the doctor in using the instrument that decides the final outcome. It is better to have a dual chest piece stethoscope with the bell and diaphragm. The former is more useful to auscultate low pitched sounds and murmurs, whereas the latter performs better for high-pitched murmurs and sounds. Pediatric stethoscopes are also available. The tube of the stethoscope should be 25 cm long for ideal reception. The ear pieces should fit snugly into the auditory canal without causing undue tension and pain. Once the appropriate stethoscope is selected, the doctor should gain experience with it to perfect the auscultatory method and to identify normal and abnormal findings.

Areas over the precordium where events taking place in the heart are best heard:

Mitral area: For example, over the area of normal apex beat, i.e. fifth left intercostal space 1.5 cm internal to the left mid clavicular line.

Tricuspid area: Fifth left intercostal space close to the sternum.

Pulmonary area: Second left intercostal space close to the sternum.

Aortic area: Second right intercostal space close to the sternum.

Second aortic area: Third left intercostal space close to the sternum (Figs 15.24 A to H).

Procedure

With the patient lying supine or sitting up, auscultate all the areas systematically. Try to identify the auscultatory events—normal and abnormal. Once they have been identified, assess the quality and intensity. If abnormal events such as murmurs are present identify the direction and extent of conduction. Conclude auscultation by noting the changes produced during the different phases of respiration and by adopting different postures.

Points to Note in Auscultation

1. Heart sounds—character, intensity, splitting rhythm
2. Adventitious sounds
3. Murmurs, if present their intensity, character and propagation
4. Relationship of auscultatory events with the respiratory cycle
5. Change with alteration in position of the patient and exercises.

Normal Auscultatory Events

Heart sounds: There are four heart sounds which can be picked up by the trained ear (Fig. 15.25).

First heart sound: This is produced by closure of the atrioventricular valves and synchronizes with the end of diastole and the onset of ventricular systole. First heart sound is low pitched and it resembles phonetically the sound "lubb". This is best heard over the mitral area.

Second heart sound: This is produced by closure of the semilunar valves and synchronises with the end of systole and onset of ventricular diastole. This sound is sharp, high pitched and shorter in duration resembling the sound "dup". This is best heard over the aortic area.



Figs 15.24A to H: Auscultatory areas: (A) mitral, (B) tricuspid, (C) pulmonary, (D) aortic, (E) second aortic area, (F) conduction of mitral systolic murmur (arrow), (G) conduction of aortic systolic murmur (arrow), (H) conduction of aortic diastolic murmur

Third heart sound: This is heard during the early part of diastole and is produced by rapid inflow of blood from the atria into the ventricles. It is a low pitched soft sound heard at the mitral area and also medial to it.

In childhood and hyperdynamic states such as pregnancy and anemia, third heart sound may be well-heard. In disease states such as cardiac failure and cardiomyopathy, presence of abnormal third heart sound may denote diastolic dysfunction of the ventricular myocardium.

Fourth heart sound: This is caused by atrial contraction and occurs in late diastole. It is soft and low pitched and considerable training is needed to appreciate it. Fourth heart sound becomes prominent in conditions in which forceful atrial contractions are necessary for proper ventricular filling such as ventricular hypertrophy due to hypertension, outflow obstruction or cardiomyopathy.

Note: Before proceeding with auscultation on patients, the beginner should auscultate normal subjects and identify the heart sounds, their quality and the timing of systole and diastole. Look for the following:

Heart rate: Count for one minute with auscultation over the cardiac apex. Generally, the pulse rate and heart rate are equal. In many conditions such as atrial fibrillation and extrasystole some of the contractions of the heart may not be transmitted as pulse. In these the stroke volumes for beats occurring at shorter diastolic intervals are inadequate to produce a pulse. This phenomenon is called pulse deficit. To get the pulse deficit accurately at any given time two observers have to count the heart rate and pulse rate independently at the same time and find out the difference. This is so, because in conditions such as atrial fibrillation and extrasystoles the pulse deficit varies from time-to-time.

Abnormalities of Rhythm (Arrhythmia)

In health the heart beat is regular with only slight variation during the phases of respiration. During inspiration the rate increases and during expiration it decreases. This rhythmic alteration in heart rate with the phases of respiration is called sinus arrhythmia. Sinus arrhythmia is more prominent in children. Vagotonic individuals and those who are accustomed to heavy exertion may have slow heart rates and marked sinus arrhythmia. Autonomic neuropathy occurring in diabetes mellitus tends to abolish sinus arrhythmia. Arrhythmias may be regular or irregular.

Types of Arrhythmias

- Physiological—sinus arrhythmia.
- Pathological—may be regular or irregular.

Regular Arrhythmias: There is a basic regularity in the pattern of arrhythmia, e.g. regular extrasystole, as in ectopic bigeminal or trigeminal rhythms, partial heart block (second degree) in which a beat will be missed at regular intervals.

Irregular arrhythmias: For example, atrial fibrillation. The rhythm is irregularly irregular. The time interval between beats, strength of contraction and the intensity of heart sounds vary. All these features are reflected in the pulse also as irregularity in rhythm and force.

In *atrial flutter* the atrium contracts at rates of 250 to 300/minute but atrioventricular block develops and therefore ventricular rhythm is slower and regular. If the A-V block varies, the ventricular rhythm becomes irregular.

Ventricular Extrasystoles

Extrasystoles occur irregularly. They are produced by impulses arising from ectopic foci in the ventricles. Only those impulses reaching the myocardium after the absolute refractory period of the previous beat elicit contractions. The strength of contraction depends on the time at which the impulse occurs in diastole. Ectopic beats that fall in the earlier phases of diastole are weaker than those occurring in the later phases. Since the extrasystole blocks the regular impulse following it, a compensatory pause follows. This is the hallmark of extrasystoles. The interval between the normal beats preceding and following the ectopic beat is about twice that of the normal cycle length.

Pulsus Bigeminus

It is the rhythm in which two beats occur in succession, followed by a pause. This happens when an extrasystole follows every normal beat, as in digitalis toxicity. Another cause of pulsus bigeminus is a heart block in which every third beat is missed, i.e. sinoatrial (SA) block or atrioventricular (AV)

block with a 3:2 conduction ratio. Yet another cause is sick sinus syndrome where a junctional escape followed by a sinus capture produces an escape-capture bigeminal rhythm.

Effects of Exercise

Once an arrhythmia is detected, if the patient's condition will permit, he is made to exercise by sitting up in bed and lying flat 3 to 5 times. Atrial fibrillation becomes more irregular while benign ventricular extrasystoles tend to disappear. Heart block is generally unaltered by exercise.

Occurrence of ventricular or supraventricular extrasystoles in runs gives rise to paroxysmal tachycardias. In these, the rates generally vary from 120 to 180/minute. If these episodes last longer than 30 seconds they are called sustained tachycardias, while shorter ones are referred to as non-sustained tachycardias.

Intensity of Sounds

The first and second heart sounds are both loud in tachycardias and physiological states with increased cardiac output. In persons with thin chest wall naturally the heart sounds are louder compared to obese subjects. In emphysema where the lungs cover the heart, and pericardial effusion where fluid is interposed between the heart and the chest wall, the transmission of sounds is diminished.

In hypovolemic conditions such as shock and in conditions where systolic contraction of the heart is weak as in myocarditis and severe grades of cardiac failure, the first sound may become weak and soft.

In valvular diseases where proper closure of the valve in systole or diastole is defective, the corresponding heart sound may be altered. For example, in mitral and tricuspid incompetence where the A-V valves fail to appose properly the first sound tends to be weak. In aortic and pulmonary stenosis the diastolic pressure in the corresponding great vessel is comparatively lower, resulting in weaker closure of the semilunar valves and consequent diminution in intensity of the second sound. In aortic and pulmonary incompetence, the second sound tends to be weak due to failure of closure of the semilunar valves at the onset of diastole.

Triple Rhythm

This is not an arrhythmia. The third and fourth sounds become prominent in several conditions. Third heart sound is accentuated in conditions of increased ventricular filling such as mitral incompetence and tricuspid incompetence. In cardiac failure the third and fourth sound may become prominent. The fourth heart sound may be audible when atrial contraction becomes forceful as a result of reduced ventricular compliance.

When the third or fourth heart sound becomes prominent and audible, the cadence of three heart sounds for each cardiac cycle is called triple rhythm. Triple rhythm may be physiological as is seen in children and pregnant women in whom the third heart sound is audible, or it may be abnormal as in cardiac failure. When triple rhythm is associated with tachycardia and other abnormalities of the heart, it is called gallop rhythm. Gallop rhythm may be due to the presence of S_3. This is called early diastolic or protodiastolic gallop.

Prominence of S_4 gives rises to a late diastolic, or presystolic gallop. Summation gallop is the term used to denote the condition in which S_3 and S_4 tend to merge as a result of gross reduction in diastole caused by tachycardia. Apart from cardiac failure, gallop rhythm may occur in ischemic heart disease, cardiomyopathy, and myocarditis.

Clicks

These are sharp short sounds produced in systole. Clicks may be valvar in origin, and associated with ejection of blood across diseased semilunar valves into the great vessels, as in aortic or pulmonary stenosis. However ejection clicks may also be due to sudden stretch of the arterial walls as in pulmonary hypertension or idiopathic dilatation of pulmonary artery. Clicks may also be nonejection in nature, as in mitral valve prolapse due to the billowing action of the mitral valve in systole.

Opening Snap

This is a sharp snapping sound, heard in mitral stenosis when the stenotic mitral valve which is flung open is brought to an abrupt halt. This occurs in the earlier part of diastole and it is followed by the mid-diastolic murmur.

Extracardiac Sounds

Pericardial knocks may be heard in constrictive pericarditis. In pneumothorax the collapsed lung may knock against the mediastinum and produce low pitched sounds.

Quality of the Sounds

More than intensity, it is the quality of sounds that are more helpful in diagnosis. Clicks, snaps and extracardiac sounds have distinct qualities which help them to be identified from each other and from normal heart sounds. Clicks and snaps are high-pitched and sharp. Extracardiac sounds vary in pitch. Timing their occurence in the cardiac cycle is also helpful for identification.

Splitting of Sounds

Though the first and second heart sounds are generally described as single, both are formed by the fusion of the sounds produced by the valves on the right and left sides of the heart which close slightly asynchronously. Since both aortic and pulmonary components of the second sound are heard well over the pulmonary area, splitting is best heard here. Normally the aortic and pulmonary components of the second sound, produced by closure of the corresponding semilunar valves are seen to come closer during expiration and separate out during inspiration. The right ventricle takes a slightly longer time for complete ejection during inspiration and therefore the pulmonary component of the second sound is delayed. During expiration the pulmonary valve closes earlier than during inspiration, and aortic ejection takes a bit longer time. Therefore, the split of the second sound disappears normally. This phenomenon of split occurring during inspiration and closing during expiration is called "normal split" (Fig. 15.25).

When the split is more pronounced, it is called "wide split". This happens when the right ventricle takes a longer time to complete ejection, as in right ventricular volume overload conditions. When the respiratory variability in the split is abolished, it is called "fixed split". This is typically seen in atrial septal defect, since in this condition the blood flowing through the pulmonary artery is considerably more than the flow in the aorta and also it remains more or less unchanged during the two phases of respiration.

If the split in the pulmonary area becomes narrower during inspiration and wider during expiration, it is called "reverse split". This happens in conditions where the left ventricle ejects blood against resistance such as in hypertensive cardiac

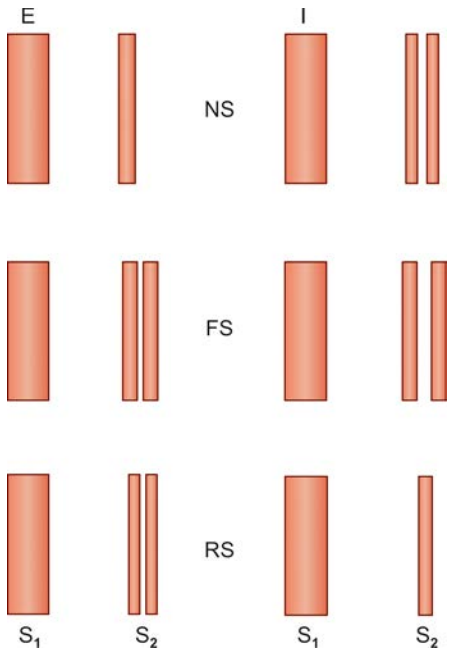


Fig. 15.25: Diagram showing splitting of second heart sound in the pulmonary area: E–expiration, I–inspiration, NS–normal split, FS–fixed split, RS–reversed split

disease or aortic stenosis. In this condition, the aortic component of the second sound falls after the pulmonary second sound. During inspiration pulmonary valve closure gets delayed and therefore comes closer to the aortic second sound, thereby narrowing the gap between the two components. Reversed split may also be seen where left ventricular activation is delayed as in left bundle branch block.

Prosthetic Valve Sounds

Insertion of prosthetic cardiac valves may give rise to special auscultatory findings. Biologial valves produce sounds similar to the natural valves. Artificial mechanical valves usually produce two sounds or clicks for each cardiac cycle—an opening click and a louder closing click.

Disappearance or muffling of these sounds give indication of thrombosis or other abnormalities in these valves.

Adventitious Sounds

These are *murmurs and rubs*. Blood flow across a normal valve or in a normal artery does not cause audible adventitious sounds, since the valve orifice

and arterial lumen are sufficient to allow smooth flow. Moreover the endothelial surfaces are regular and smooth so that abnormal eddies or vibrations do not occur. When valve orifices are narrowed, surfaces are roughened, or the flow of blood through them is excessive, abnormal vibrations occur and these lead to murmurs. When valves become incompetent, the blood leaks back through them and this abnormal blood flow also leads to murmurs. Though the normal flow of blood is inaudible to the unaided human ear, the vibrations can be made audible by Doppler echography.

Murmurs may be organic or functional: Organic murmurs are caused by anatomical abnormalities of valves or arteries, whereas functional murmurs are caused by purely hemodynamic factors.

When a murmur is detected, try to ascertain the following points by auscultation.

1. *What is its timing?* Systolic, diastolic or continuous—if systolic or diastolic, whether it occurs throughout systole or diastole, or occupies only part of these phases.
2. *When does it start and what is its duration?*

Murmur that starts a little while after the first heart sound, increases in midsystole and dies out before the second sound, is called midsystolic murmur or ejection murmur, because the timing and intensity of the murmur closely follow the timing and dynamics of ventricular ejection.

If the murmur occupies the latter half of systole it is called a late systolic murmur (Fig. 15.26).

Murmur commencing with the first sound and continuing throughout systole up to the second sound is termed pansystolic murmur (Fig. 15.27).

Diastolic murmur that starts along with the second heart sound is called early diastolic murmur. It may extend through variable periods into diastole. Such murmurs are heard in aortic incompetence and pulmonary incompetence (Fig. 15.28).

Murmurs that start in mid-diastole, i.e. a while after the onset of diastole are called mid diastolic murmurs. These may extend for variable periods during diastole. If they exist till late diastole they are termed as presystolic. If during this period there is accentuation of the murmur, it is called presystolic accentuation. This is seen in mitral stenosis with normal sinus rhythm.

3. *What is its quality?* Murmurs may be high pitched and blowing in type, or low pitched and rough. Blowing murmurs are characteristic of abnormal blood flow from high pressure areas to

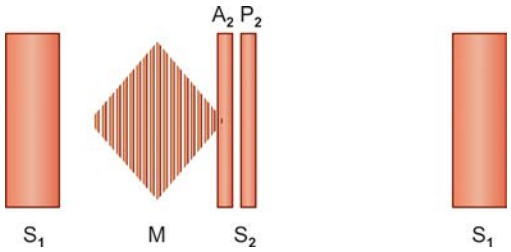


Fig. 15.26: Ejection systolic murmur of aortic stenosis: S_1–First heart sound, S_2– Second heart sound, P_2– Pulmonary component, A_2– Aortic component, M–Murmur

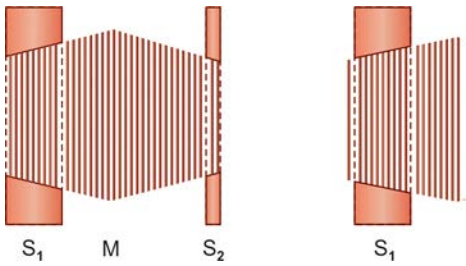


Fig. 15.27: Pansystolic murmur of mitral regurgitation

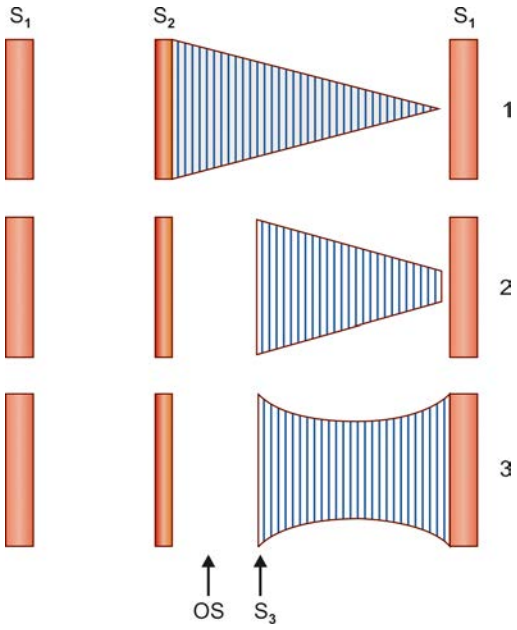


Fig. 15.28: Diagram showing time relationship of diastolic murmur: S_1–first heart sound, S_2–second heart sound, OS–position of opening snap, S_3–position of third heart sound, 1–early diastolic murmur, 2–mid-diastolic murmur, 3–mid-diastolic murmur with presystolic accentuation

low pressure areas with high velocity and force, e.g. (1) Mitral incompetence and tricuspid incompetence in which blood flows from ventricles into atria during systole. (2) Blood from the aorta or pulmonary artery leaking into the ventricles in diastole in incompetence of the corresponding valves.

In ventricular septal defect the high pitched pansystolic murmur is produced by blood flowing from the left ventricle to the right ventricle across the defect, under high pressure.

The smaller the orifice, greater is the intensity and pitch of the murmur. Murmurs tend to be low pitched and rough if they are produced by blood flow across roughened surfaces or if the pressure gradient is small. The murmurs of mitral and tricuspid stenosis are typically low pitched and rumbling, since the pressure gradient is small. In aortic and pulmonary stenosis the systolic murmur tends to be low pitched and rough since the valve surfaces are roughened.

4. *What is its intensity?* Murmurs can be graded depending upon their intensity.
 - Grade 1: Faint murmur heard by an experienced observer in a quiet room after prolonged auscultation.
 - Grade 2: Faint, but definite murmurs heard from the beginning of auscultation.
 - Grade 3: Moderately loud.
 - Grade 4: Louder murmur associated with thrill
 - Grade 5: Loud murmur with thrill, can be heard, even with the rim of the stethoscope.
 - Grade 6: Loud murmur with thrill which can be heard even when the stethoscope is not in contact with the chest wall.

Though the intensity of the murmur can be graded for descriptive purposes it does not help to assess the hemodynamic abnormality. The severity of lesion and intensity of murmur do not correlate at all times. For example, in severe mitral stenosis, the mid-diastolic murmur may even be absent, and in severe aortic incompetence the early diastolic murmur may be only faint and short.

5. *What is the direction of conduction?* Murmur may be conducted along specific directions. This helps to identify the source of the murmur.

Method: Once the murmur is identified, move the stethoscope along the classic directions of conduction. If the murmur is heard with the same or even increasing intensity as one proceeds away from the site of production it is said to be conducted in that direction.

Mid-diastolic murmurs occurring in mitral stenosis and tricuspid stenosis are not conducted. Pansystolic murmur of mitral incompetence is conducted laterally to the axilla and even as far behind as the scapular angle or back. Tricuspid systolic murmur may also be conducted to the angle of the scapula or back. The ejection systolic murmur of aortic stenosis is conducted up along the carotids. At times it may be conducted to all other areas as well. Early diastolic murmur of aortic incompetence is conducted down to the epigastrium along the left and right borders of the sternum.

Pulmonary systolic murmur may be conducted upto the left clavicle. Pulmonary diastolic murmur may be heard over a short distance only to the left of the sternum in the third and fourth intercostal spaces.

Conduction of the systolic murmur of mitral valve prolapse depends upon the valve leaflet maximally affected and the direction of the regurgitant stream. It may be conducted towards the axilla in prolapse of the anterior leaflet and medially in prolapse of the posterior mitral leaflet.

6. *What is the change in the murmur with change of position of the patient?* Murmurs arising from the mitral valve are heard better in the left lateral position. Murmurs arising from the tricuspid valve are heard best in the supine position with lower limbs elevated. Aortic and pulmonary murmurs are best heard with the patient sitting up and leaning forward. The murmur of mitral valve proapse diminishes during squatting and becomes more prominent on standing.
7. *What is the effect of the phases of respiration on the intensity of the murmur?* Murmurs arising from the left sided valves become more audible on expiration while those better heard during inspiration usually originate from the right side.
8. *What is the effect of isometric exercises on the intensity of the murmur?* Make the patient tighten

his fist strongly or clench his teeth. The systolic murmur of hypertrophic cardiomyo pathy and mitral valve prolapse decreases with exercise (Tables 15.5 and 15.6).

Table 15.5: Direction of blood flow and the murmurs produced in the common cardiac lesions

Acquired valves lesions	*Direction of blood-flow normal or abnormal*	*Murmur produced and optimum site for auscultation*
Mitral stenosis	Normal	Mitral mid-diastolic murmur—Apex
Mitral incompetence	Abnormal from LV to LA	Mitral pansystolic murmur—Apex and back
Tricuspid stenosis	Normal	Tricuspid mid-diastolic murmur—Tricuspid area TA
Tricuspid incompetence	Abnormal from RV to RA	Tricuspid pansystolic murmur—Tricuspid area TA
Aortic stenosis	Normal	Midsystolic murmur aortic area along the carotid artery in the neck
Aortic incompetence	Abnormal from aorta to LV	Early diastolic murmur—aortic area down along the left and right border of the sternum
Pulmonary stenosis	Normal	Midsystolic murmur—pulmonary area
Pulmonary incompetence	Abnormal from PA to RV	Early diastolic murmur pulmonary area and down the left side of the sternum
Congenital lesions		
Ventricular septal defect	Abnormal from LV to RV	Pansystolic murmur in the third left intercostal space
Atrial septal defect	Abnormal	Pulmonary svstolic murmur due to increased flow pulmonary area (PA) Tricuspid diastolic murmur due to increased A-V flow Tricuspid area (TA)
Patent ductus arteriosus	Abnormal	Continuous murmur increasing in intensity during systole, blood always flowing into the pulmonary artery from the aorta 2nd and 3rd left intercostal space
Mitral valve prolapse	Abnormal	Systolic click with early or long systolic murmur—mitral area

Pericardial Rub

This is heard over the precordium as a leather creaking sound, during all phases of the cardiac cycle. The rub is better heard towards the upper part of the precordium and when the patient leans forward. The rub may be coarse or fine and squeaky. Pressure with the stethoscope enhances the rub. When pericardial effusion occurs, it disappears.

Pleuropericardial rub: It is heard when the breath is held in inspiration. It disappears when the breath is held in expiration.

Arterial Bruits

Auscultation over normal arteries in which blood flow is considerably increased (thyroid arteries in primary thyrotoxicosis) or where the lumen is narrowed (e.g. carotid stenosis), may reveal systolic bruit. Common sites for auscultation include the carotid arteries and vertebral arteries in the neck, renal arteries in renal artery stenosis, intercostal arteries in coarctation of aorta and any other artery in which abnormal blood flow is suspected.

Venous Hum

This is a continuous sound heard over major veins when blood flow is increased. Venous hum may be heard over the root of the neck (jugular vein) in anemia. This is known as *bruii-de-diable (devil's murmur*). The hum disappears if the jugular vein is occluded from above.

Venous hum may be heard over the umbilical vein over midline of the abdomen in cirrhosis liver with portal hypertension—Cruveilhier-Baumgarten syndrome.

RECORDING BLOOD PRESSURE

(See also Chapter 2)

Different types of sphygmomanometers are available. The mercury type is the more reliable standard instrument. It is preferable to the anaeroid type, since the latter may lose its accuracy. Anaeroid types should be checked by comparison with mercury sphygmomanometer at least once a month. Electronic instruments which give out "beep" signals are available. These are more expensive, but more convenient for self-monitoring of blood pressure. Automatic and continuous recording of blood pressure is a facility provided in most of the central

Table 15.6: Diagnostic features of the common valvular and congenital anomalies of the heart

	Apex beat	*Cardiomegaly*	*Thrill*	*Auscultation*	*Remark*
Mitral stenosis	Tapping	nil	diastolic	Loud first sound, opening snap, mid-diastolic murmur with presystolic acentuation, not conducted, heard best in mitral area (MA)	Presystolic accentuation disappears when atrial fibrillation sets in
Mitral incompetence	Forceful	+	+ systolic	First sound soft and continuous with pansystolic murmur, heard best in MA, high pitched, conducted to axilla	Often third heart sound, and a short mid-diastolic rumble due to excessive diastolic flow into left ventricle, are present.
Aortic stenosis	Heaving	±	systolic	Ejection systolic murmur heard over AA conducted to carotids, faint aortic second sound with reversed split	The intensity and duration of murmur come down when force of contraction of left ventricle comes down as in cardiac failure.
Aortic incompetence	Forceful	++	+ diastolic	Early diastolic blowing murmur heard over AA conducted down to the epigastrium. Sometimes systolic murmur due to increased flow. Soft aortic second sound except in syphilitic aortitis where it may be ringing	Peripheral auscultatory signs. Pistol shot sounds. Duroziez murmur. In many cases of pure aortic incompetence, due to pressure of the regurgitant stream of blood on to the —mitral valve cusps a functional mitral mid diastolic murmur develops—the Austin Flint murmur. Unlike in mitral stenosis, the first heart sound is not loud and apex not tapping.
Pulmonary stenosis	Normal	Nil	systolic	Ejection systolic murmur heard over PA conducted up to left clavicle, soft pulmonary second sound, with wide splitting and inconstant ejection click	Left parasternal heave present
Pulmonary incompetence	Normal	±	± diastolic	Early diastolic murmur often starts after a loud pulmonary second sound heard in the pulmonary area. Functional diastolic murmur in PA is known as Graham Steell's murmur	Murmur increases with inspiration
Tricuspid incompetence	Variable	+	±	Pansystolic murmur heard over TA increasing with inspiration, over tricuspid area	Pulsatile liver present, pulsations increase with inspiration, prominent "V" waves in the JVP with sharp "Y" descent.
Tricuspid stenosis	Normal	±	diastolic	Mid-diastolic murmur heard over TA over tricuspid area	Often associated with giant "a" waves in jugular venous pulse
Ventricular septal defect	Forceful	±	systolic ++	Pansystolic murmur 3rd and 4th left intercostal spaces murmur	Larger the septal defect, less intense is the murmur. Associated flow across mitral valve and / or aortic incompetence may be present
Atrial septal defect	Normal or forceful	+	systolic thrill in pulmonary area	Fixed split of pulmonary second sound—often ejection systolic murmur over pulmonary area	In ostium primum type there is associated mitral incompetence. Flow murmur across the tricuspid valve (mid diastolic)
Patent ductus arteriosus	Normal or forceful	±	Continuous thrill	Continuous murmur (machinery murmur) over the second left intercostals space	When pulmonary hypertension develops the diastolic component comes down, later the murmur becomes less characteristic
Mitral valve prolapse	Normal	Nil	Nil	Early systolic click and late systolic mummur over mitral area	Heard better when standing than during squatting

Note: MA - mitral area, AA - aortic area, PA - pulmonary area, TA - tricuspid area

monitoring equipment available in cardiac intensive care units.

For clinical use the routine is to record the blood pressure in the right arm unless there is any contraindication. If the arm is paralysed, the recording should be done on the normal limb, since values are likely to be lower on the paralysed side. Separate cuffs are available for adults and children and the appropriate cuff should be used to avoid errors. The rubber bag of the ordinary cuff used for adults is 12 cm wide and 25 cm long.

Procedure

The cuff should be tied tight around the arm over the brachial artery, leaving the cubital fossa free for auscultation. The cuff is inflated while palpating the radial pulse (or brachial pulse), till the pulse is obliterated. The point at which the pulse reappears on deflating the cuff is noted. This gives an idea about the approximate systolic pressure. Usually the systolic pressure determined by the palpatory method is 10 to 15 mm Hg below that obtained by auscultation.

Inflate the cuff 30 to 40 mm above the level of systolic pressure obtained by palpation. Slowly deflate the cuff at the rate of 5 to 10 mm/second, while auscultating over the cubital fossa. The first appearance of *Korotkoff's sounds* over the brachial artery is taken as the *systolic blood pressure*. Continue to release the pressure till the sounds disappear. This is taken as the diastolic blood pressure. This procedure is done thrice and the lowest figure obtained is taken to represent the actual value. The difference between the systolic and *diastolic blood pressures* is the pulse pressure. When one-third of the *pulse pressure* is added to diastolic blood pressure we get the *mean arterial pressure*. The disappearance of sounds (phase V of Korotkoff's sounds) is now widely accepted as the diastolic pressure for reproducibility of results and to minimise interobserver variation. Blood pressure is expressed conventionally as the height of mercury column in mm Hg. It is expressed as kilopascals (kpa) in SI units (1 kpa = 7.5 mm Hg approximate).

The Joint National Committee (JNC, USA) periodically revises the criteria for normal blood pressure readings and different grades of hypertension. The currently followed JNC-VII guidelines have proposed that the normal systolic blood pressure in adults is below120 mm Hg and normal diastolic blood pressure is below 80 mm of Hg. Systolic BP values above 140 mm Hg diastolic readings above 90 mm Hg indicate hypertension. Values in the range of 120 to 139 systolic and 80 to 89 diastolic indicate prehypertension, whose lifetime risk of developing hypertension is estimated to be 90%. Finally as per the JNC-VII, systolic BP above 160 mm Hg and diastolic BP above 100 mm Hg indicates stage II hypertension very often needing combination drug therapy for optimal control. Most patients with hypertension have an elevation of both systolic and diastolic pressures. If *systolic pressure* alone is elevated, it is called isolated systolic hypertension (ISH). ISH is common in the elderly and the wide pulse pressure seen in this form of hypertension carries a very poor prognosis. If diastolic pressure alone is elevated it is called diastolic hypertension. This is the least common form and is seen in young adults

The blood pressure is lower in children below the age of 10 years. From the age of 14 years till the age of 60, the blood pressure remains almost the same in healthy individuals.

When any variation from normal is obtained, it is advisable to take the blood pressure in both arms. In normal subjects the difference between the two arms does not exceed 10 mm Hg systolic. For diastolic pressure the difference is even less. If there is greater disparity, the higher values should be taken as the actual pressures. Arterial occlusion due to any reason lowers the blood pressure in the limb.

To take the blood pressure in the lower limb, the patient lies prone with the leg partly flexed and supported on a pillow. The cuff is applied around the lower third of the thigh and auscultation is done over the popliteal fossa. If available, a larger cuff is preferable. In normals, the pressure recorded in the thigh is 20 to 30 mm Hg above that obtained in the arm. This is partly an artefact, on account of the greater muscle mass of the thigh. Blood pressure should be recorded in the lower limb under the following clinical indications:

1. Radiofemoral pulse delay, or weakness of femoral or dorsalis pedis pulse.
2. Aortic regurgitation.

In obstruction to the aorta as in coarctation or aortoarteritis, the blood pressure in the thigh is considerably lowered. In aortic regurgitation the

systolic pressure recorded at the thigh tends to exceed that in the upper limb by 20 mm Hg or more. This is termed Hill's sign.

Fallacies in Recording Blood Pressure

Auscultatory gap: In some individuals with high systolic pressures, when the pressure in the cuff is lowered, the sounds appear at the systolic level disappear over a segment and reappear again, to disappear finally at the diastolic pressure. This gap of silence in the systolic pressure is called the auscultatory gap. If the pressure in the cuff is not elevated above the level of auscultatory gap, the lower level of the auscultatory gap may be mistakenly taken as the systolic pressure. This is avoided by doing the palpatory method first.

Looseness of the cuff: If the cuff is tied loose, the pressure recorded tends to be slightly higher.

Cuff size: If the optimum sized cuff is not used, values tend to vary. Smaller cuffs give higher values.

Anxiety: If the patient is apprehensive, the recorded pressure tends to go high, systolic much more than diastolic. With repeated recording the values keep on coming down, though not to base line levels. Such patients may require mild sedation and conditioning by repeated recordings. The term "***casual blood pressure***" or "office blood pressure" is used to denote the values obtained when the patient is examined at the doctor's clinic without any prior preparation. "Basal blood pressure" is obtained after making the patient rest for about an hour in bed, and a sedative like 5 mg of diazepam administered to allay anxiety. For epidemiological work and routine clinical use the office blood pressure is fairly reliable. The term ***white coat hypertension*** denotes the elevation of blood pressure caused by fear and apprehension when the doctor records the pressure. For routine clinical use, the office blood pressure record, repeated 2 or 3 times on different days is adequate. In a few cases where reliable information is not obtained and where factors such as anxiety, exertion or drug effect tend to alter the recorded blood pressure values, 24 hours blood pressure recording can be done by appropriate ambulatory portable recording instruments. This should be done for proper evaluation.

For more accurate observations specialized instruments such as "random zero sphygmo manometer" are available.

Abnormally low blood pressure: This occurs in shock. Often the Korotkoff's sounds may not be audible or they may be audible only over a very narrow range and hence likely to be missed. In such cases the palpatory method over the bronchial artery may help.

Paroxysmal hypertension: The fluctuation in blood pressure may be paroxysmal, as is seen in the early phases of pheochromocytoma. This can be identified only by repeated recordings or by 24 hr ambulatory blood pressure recording.

Postural variations: The blood pressure values recorded with the patient lying in bed are accepted for routine use. In the erect posture the systolic pressure may remain the same or fall by up to 10 mm Hg, the diastolic remaining the same. If on standing, the pressures drop more than 10 mm Hg with symptoms, or by more than 20 mm Hg, this is termed postural hypotension.

Recording of blood pressure is a very reliable objective method to study one of the most important functions of the cardiovascular system. Since hypertension is a very common malady and many of these patients are asymptomatic, recording of blood pressure is the only method to bring them to light. Hence the importance of learning the technique and its interpretation cannot be overemphasized. Hypertension is prevalent among 15 to 30% of the population and thereby it is one of the common afflictions of mankind. Cardiac failure, ischemic heart disease, fatal arrhythmias, cerebrovascular accidents, renal failure and several other diseases are directly related to hypertension. Prompt reduction of blood pressure is the most effective way to prevent all these complications. Hence the importance of recording the blood pressure at every visit cannot be overemphasized. Though the sphygmomanometer method is adequate for all routine clinical use, for more delicate and accurate recordings, required for anesthesia, major surgery and the like, intra-arterial pressures are recorded, using sophisticated instruments.

Clinical examination of the cardiovascular system is completed with the following examinations. Look for evidences of cardiac failure.

1. Right sided heart failure:
 a. Engorged jugular vein
 b. Enlarged tender liver
 c. Dependent edema.

2. Left sided heart failure:
 a. Tachypnea, cheynes stokes respiration
 b. Pulsus alternans
 c. Gallop rhythm
 d. Basal crepitations in the lungs.

Arterial occlusion: By palpating over the major arteries and looking for the temperature and color of the limbs.

Venous occlusion and inflammation: Look for distal oedema and tender and palpable veins. In the legs look for Homans sign, i.e. passive dorsiflexion of the foot with legs straight, causes pain over the calf. This suggests deep vein thrombosis in the calf.

Ophthalmoscopy

Look for signs of hypertension, infective endocarditis, hyperviscosity states and others (See Chapter 48).

CHAPTER

16 Investigations in Cardiology

K Suresh, KV Krishna Das

Electrocardiography, Systemic investigations, Radiological investigations, Cardiac ultrasonography, Coronary angiography, Computed tomography, Magnetic resonance imaging, Nuclear imaging, Positron emission tomography, Cardiac catheterization

ELECTROCARDIOGRAPHY

The electrocardiogram (ECG) is a graphic record of the electrical activity of the heart and it is recorded by the electrocardiograph.

General Considerations

In modern clinical practice, the ECG has come to stay as a readily available tool to diagnose and manage many cardiac and noncardiac conditions. It is a part of the diagnostic equipment of all doctors ranging from the primary care physician to the cardiologist. Hence it is essential that all doctors should understand its principles and application.

Ionic Basis for Cardiac Electrical Activity
Resting Membrane Potential

In the resting state a potential difference exists across the cell membrane of myocardial cells. The basis for this resting membrane potential (RMP) is the differential distribution of ions across the cell membrane.

Movement of ions across the cell membrane is influenced by 3 factors:

1. The ions move from regions of higher concentration to those of lower concentration. The electric gradient allows charged ions to diffuse along their electric gradient.
2. The cell membrane is selectively permeable permitting free passage of smaller ions like K^+, while restricting movement of other ions like Na^+.
3. The interior of the cell has a high concentration of potassium ions (K^+) and protein anions, while the cell exterior is rich in sodium (Na^+) and chloride (Cl^-) ions.

The RMP is generated and maintained by the selective permeability of the cell membrane to potassium, which tends to diffuse out from the cell along its concentration gradient. This movement is opposed by the positive electrical charge of the cell exterior. The cell exterior has a positive charge due to the activity of the sodium-potassium ATPase pump which actively pushes out the sodium from the cell by an energy dependent process. A net equilibrium is struck between these opposing forces, so that the cell interior is negative in the resting state. In most cardiac cells the resting membrane potential is about –60 to –90 millivolts (mV).

Action Potential

An action potential develops in response to any stimulus that produces changes in the ionic permeability of the cell membrane. Such stimuli produce alteration in the physicochemical environment which modify the permeability of the cell membrane. The action potential consists of depolarization and repolarization processes.

Depolarization

This is also referred to as phase-0 (spike phase) of the action potential. In response to a stimulus, the Na^+ channels in the cell membrane open up allowing

free entry of sodium into the cell. The cell interior becomes slightly positive (+30 mv) at the peak of phase-0 and this reversal of polarity leads to closure of the Na^+ channels. Depolarization is a passive process.

Repolarization

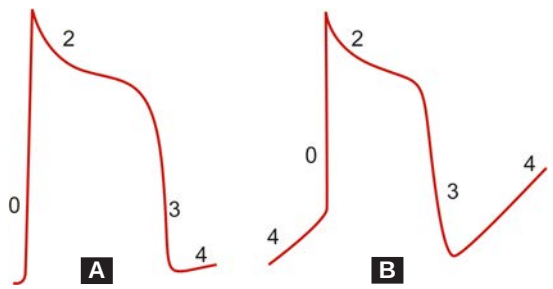
Restoration of the resting membrane potential is a much longer process. It is an active, energy dependent process, consisting of four phases:

Phase 1: (Overshoot phase) is the reversal of the overshoot and return of the membrane potential to 0 mv. This initial sharp early repolarization is achieved by an increase in the entry of chloride ions into the cell (Figs 16.1A and B).

Phase 2: (Plateau phase) of the action potential is the time when calcium channels open up allowing influx of calcium ions (Ca^{++}) into the cell. This influx of Ca^{++} is neutralized by an outward efflux of K^+ so that the membrane potential remains at a plateau.

Phase 3: (Cascade phase) is the phase of repolarization mediated by continuing K^+ efflux which re-establishes the intracellular negativity to resting levels.

Phase 4: (Resting phase) For each action potential, some Na^+ ions enter the cell during depolarization and some K^+ ions are lost during repolarisation. Restoration of the appropriate intracellular and extracellular concentrations of Na^+ and K^+ is achieved by an energy dependent ionic pump during phase 4. The excess Na^+ ions are pumped out in exchange for K^+ ions.



Figs 16.1A and B: Schematic representation of action potential in (A) Working myocardial cell, (B) Specialized pacemaker cell

Specialized cells of the myocardium in the sinoatrial (SA) node and other parts of the conducting system of the heart are capable of generating spontaneous electrical activity. This property is referred to as automaticity. Generation of the pacemaker potential by spontaneous phase 4 diastolic depolarization is the mechanism responsible for automaticity. Regions of the myocardium, designed for faster conduction of impulses form the specialized conduction system of the heart.

ANATOMY OF THE CONDUCTION SYSTEM OF THE HEART

Sinoatrial Node

The Sinoatrial node (SA) node, 10 to 20 mm long, located subpericardially at the junction of the superior vena cava and right atrium, is the seat of impulse formation. It is supplied by an arterial branch which may arise from the right coronary artery in 55% of individuals or the left circumflex artery in 45%. The property of automaticity resides in the pacemaker cells (P cells) of the SA node. Under physiological conditions the SA node serves as the pacemaker for the heart, because it has the fastest rate of automaticity. All the subsidiary centers of automaticity such as the AV node, conduction pathways and heart muscle are suppressed by the SA node.

Internodal Pathways

The impulse from the SA node is conducted to the AV node through three specialized tracts—the anterior, middle and posterior internodal tracts. *These tracts consist of cells anatomically indistinguishable, but functionally distinct from ordinary myocardial cells.* A branch of the anterior tract, the Bachman's bundle, conducts the impulse to the left atrium. Atrial depolarization is achieved by radial spread of the impulse across the atrial musculature.

Atrioventricular Node

Atrioventricular node (AV) is an elliptical structure 3 to 5 mm long, located on the endocardial surface of the right side of the interatrial septum just above the septal leaflet of the tricuspid valve. It is supplied by the AV nodal artery which arises from the right coronary artery in 90% of individuals.

His Purkinje System

The bundle of His arises as a continuation of the AV node and divides into the right and left bundle branches. The right bundle branch, which is a thin stalk runs down on the right side of the interventricular septum and arborizes in the Purkinje system which is an extensive subendocardial network capable of swift transmission of the impulse to all portions of the ventricular myocardium. It supplies the free wall of the right ventricle and the right side of the interventricular septum.

The left bundle branches into the left anterior (superior) fascicle and the left posterior fascicle. The anterior fascicle terminates at the base of the anterior papillary muscle. It supplies the anterior, superior and lateral portions of left ventricle. The posterior fascicle ends at the base of the posterior papillary muscle. It supplies the posterior and inferior portions of left ventricle.

Speed of Transmission of Impulse

Atrial myocardium	800-1000 mm/sec
AV node	20 mm/sec
His Purkinje system	2000 mm/sec
Ventricular myocardium	800-1000 mm/sec

Accessory Bundles

Rarely accessory bundles may occur as congenital anomalies in some subjects. Three anatomically and electrophysiologically distinct abnormal tracts have been identified:

Kent bundle	Directly connects the atrium to the ipsilateral ventricle (atrioventricular bundle)
Mahaim fibers	Connect the lower part of AV node or His bundle to the ventricular septum (nodoventricular or fasciculoventricular bundles)
James fibers	Connect the atria with the lower part of AV node or to the His bundle (atrionodal or atriofascicular bundle)

Impulses reach the ventricle much quicker through these aberrant pathways. These accessory bundles form the anatomic basis for the various ventricular *pre-excitation syndromes.*

Principles of Surface Electrocardiography

Routine electrocardiographic recording is done by vacuum tube amplification equipment with a heated stylus that melts the wax on specially designed heat sensitive paper. More sophisticated electrocardiographs use chemical or ink writers and digitized storage and retrieval systems. They also provide online computer interaction for interpretation and diagnosis.

The human torso acts as a volume conductor transmitting about 20% of the electrical activity generated by the heart. The potential differences across the chest are picked up by the various lead systems and these produce deflections of the stylus. Current flowing towards the recording electrode produces an upright deflection and current moving away from the electrode causes downward deflection. These deflections are recorded on the moving electrocardiographic paper. The paper moves at a speed of 25 mm/sec, i.e. 1500 mm per minute. The paper is marked by horizontal and vertical lines. The vertical lines which are 1 mm apart are time lines—each interval represents 40 milliseconds at the usual paper speed of 25 mm/sec. The horizontal lines are also 1 mm apart and they indicate voltages. At normal standardization a potential difference of 1 mv produces a deflection of 10 mm so that each horizontal line denotes 0.1 mv.

Large amplitude deflections can be reduced in size and recorded by half standardization wherein 1 mv potential difference produces a deflection of 5 mm. Likewise very small complexes can be amplified by double standardization.

If the deflections of the stylus are too large or too small, there is provision to reduce or increase the excursion of the stylus by altering the standardization. So also the speed of the paper can be increased when indicated. During specialized procedures such as electrophysiologic studies and cardiac catheterization, ECG recording is done at faster paper speeds of 100 to 200 mm/second or more.

Lead Systems

A lead is a pair of electrodes, consisting of an exploring electrode and an indifferent electrode. The potential

difference between these two electrodes is recorded. Ideally the patient is in the recumbent posture and good contact between the electrode and the skin is ensured by applying electrode jelly. There are various types of lead systems.

Bipolar Limb Leads (Standard Leads of Einthoven)

The potential difference between the two electrodes is recorded in all bipolar leads. The exploring electrode is the positive pole and indifferent electrode is the negative pole. The position of the electrodes in the standard limb leads is:
Lead I: Left arm (+) to right arm (–ve)
Lead II: Left leg (+) to right arm (–ve)
Lead III: Left leg (+) to left arm (–ve) (Fig. 16.4).

Unipolar Limb Leads

Unipolar leads record the actual potential beneath the exploring electrode. This is achieved by connecting the indifferent electrode to a central terminal of zero potential which is obtained by interconnecting the left arm, right arm and left leg electrodes together. Unipolar limb leads VR, VL and VF denote the position of the exploring electrode when kept on the right arm, left arm or left foot respectively. The potentials recorded from such a system are of low amplitude. Therefore the potentials are augmented by suitable modifications. These augmented unipolar leads are denoted by the terms aVR, aVL and aVF respectively.

Unipolar Chest Leads

The indifferent electrode is connected to the central terminal, while the exploring electrode is placed at various points on the chest wall as noted below (Fig. 16.2):

- V_1 4th intercostal space near the right sternal border.
- V_2 4th intercostal space near the left sternal border.
- V_3 Midway between V_2 and V_4.
- V_4 Midclavicular line in 5th left intercostal space.
- V_5 Anterior axillary line in the same horizontal line as V_4.
- V_6 Midaxillary line in the same horizontal level as V_4.

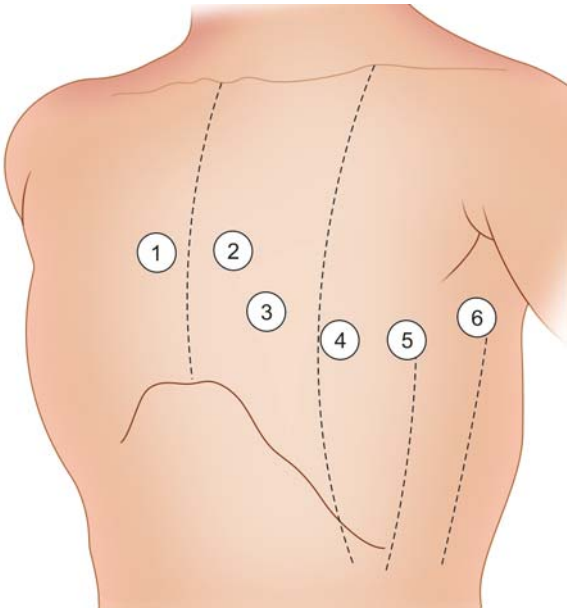


Fig. 16.2: Position of chest leads V_1-V_6

Rarely V_7, V_8 and V_9 are also recorded from further lateral areas.

These are in the same horizontal level as V_4, but along the posterior axillary line, midscapular line and posterior midline respectively. In case of cardiac malpositions and displacements V_{3R} to V_{6R} are also recorded, wherein the electrode is placed on the right side of the chest in positions corresponding to V_3–V_6.

The term high chest leads denote placement of the electrode one space above the standard chest leads and low chest leads are those placed one space below. These are used when more areas of the myocardium have to be studied, in the absence of diagnostic findings in standard chest leads.

Methods of Recording the Electrical Activity of the Heart

There are various methods of recording the electrical activity of the heart:

Scalar electrocardiography: The term "scalar" is used to describe a phenomenon which has got only magnitude, not direction. This applies to the commonly used technique of recording the ECG by keeping electrodes on the surface of the body, which is also known as the surface ECG. It records the magnitude of electrical activity generated along one plane.

Vector cardiography: In contrast to scalar electrocardiography, the vector cardiogram is the

instantaneous recording of the electrical activity of the heart along the three planes, frontal, sagittal and horizontal, during atrial and ventricular depolarization and also ventricular repolarization. The magnitude and direction of electrical activity are recorded. The Frank lead system using leads X, Y and Z in the three planes is used for vector cardiography. This is different from the leads used for scalar ECG.

Indications for electrocardiogram:

1. As the first investigation in any patient with chest pain to rule out ischemic heart disease.
2. As the gold standard for the analysis and identification of the various arrhythmias.
3. To detect abnormalities in conduction of the cardiac impulse such as bundle branch blocks, hemiblocks, accessory pathways and pre-excitation syndromes.
4. To detect the presence of atrial enlargement and ventricular hypertrophy.
5. Provides useful information about the effects of the various metabolic and electrolyte disturbances like hyper- and hypokalemia, hyper- and hypocalcemia, hypothyroidism, hypothermia, uremia and others.
6. As an essential component of intensive care monitoring.
7. For the diagnosis of acute pericarditis and pericardial effusion.
8. When myocarditis is suspected during the course of systemic illnesses like rheumatic fever, and diphtheria.
9. Drug toxicity—digitalis, daunorubicin, poisons like *Cerbera odollam*, *Nerium oleander* and others.
10. For physical fitness testing.

The Normal Electrocardiogram

P Wave

Depolarization of the atrium produces the P wave which is normally upright in standard leads. Right atrium is activated first, followed by left atrium. The P wave has a duration of 90 to 100 msec and an amplitude of 0.25 mV. The mean direction of the atrial vector is downwards and to the left so that the frontal plane P wave axis is + 30 to + 60.

By convention the first negative deflection after the P wave is called Q wave. The first positive deflection is called R wave. A negative deflection after the R wave is called S wave. A positive deflection which follows the S wave is called R wave.

PR Interval

This interval denotes the time from the onset of the P wave to the beginning of the QRS complex. It represents the time taken by the impulse to traverse the atrium (P wave), the AV node, bundle of His, bundle branches and the proximal 1/3rd of the interventricular septum (PR segment). The PR segment is isoelectric because of electrical silence after completion of atrial depolarization and entry of impulse into the AV node. Normal PR interval is 0.12 to 0.20 sec.

QRS Complex

Depolarization of the ventricles produce the QRS complex. The initial vector is due to activation of the middle third of the interventricular septum from the left to the right. This accounts for an initial R wave in right chest leads (V_1) and a small Q wave in the left chest leads (V_5,V_6). This is followed by simultaneous activation of the free walls of both ventricles. The resultant vector is directed towards the left ventricle which has a greater muscle mass producing an S wave in right sided leads and a tall R in left sided leads. Next the posterobasal portions of the left ventricle and the right ventricular outflow are activated. This final vector is again directed to the right and accounts for an R in VI and a terminal S in V_6. Components of a normal electrocardiogram are given in Figure 16.3.

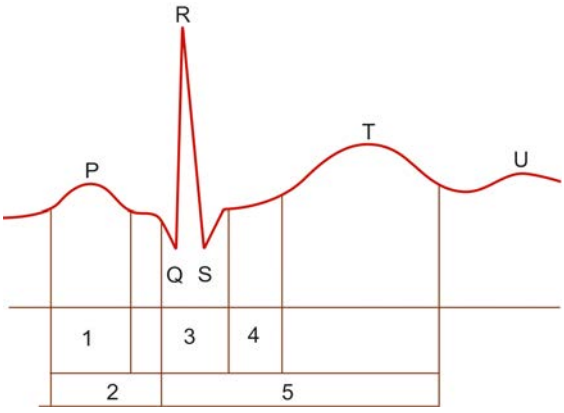


Fig. 16.3: Components of normal ECG: 1—Duration of P wave, 2—P-R interval, 3—QRS duration, 4—ST segment, 5—QT interval

Normally leads oriented to the right ventricle (V_1) record a small initial positive deflection and then a deep negative deflection referred to as the rS morphology. Leads oriented to the left ventricle record a qR pattern, viz. a small initial negative deflection, followed by a tall positive wave. This transition from the rS morphology to the qR pattern normally occurs in V_4 or V_5. If, however, the right ventricular (rS) morphology persists in the left chest leads (V_5–V_6), this is called clockwise rotation of the heart. Likewise if the left ventricular qR pattern is seen from right chest leads (V_2 or V_3), it is referred to as counterclockwise rotation of the heart. This, however, refers only to the position of the heart in relation to the horizontal plane.

J Point

This is the point where the distal limb of the S wave merges with the ST segment.

ST Segment

The isoelectric segment recorded at the end of ventricular depolarization, prior to ventricular repolarization is termed the ST segment. It lasts from the end of the QRS complex to the beginning of the T wave. Alteration of the ST segment is an important pointer to myocardial injury.

T Wave

This denotes ventricular repolarization. Although repolarization is electrically opposite to depolarization, direction of the T wave is the same as that of QRS complex. This is because the direction of spread of repolarization is opposite to that of depolarization. Whereas depolarization spreads from the endocardium to the epicardium, repolarization starts in the epicardium and spreads towards the endocardium.

QT Interval

This is the interval from the beginning of the QRS complex to the end of the T wave. It denotes the total electromechanical systole. It varies inversely with the heart rate and therefore more useful information is obtained if the QT is expressed in relation to the heart rate. This is known as corrected QT and is expressed as QTc which can be obtained by the *Bazett's formula:*

$$\frac{QT}{\sqrt{RR\ interval}}$$

Note: All values are in milliseconds.

The QT interval may be prolonged in myocardial ischemia, electrolyte imbalance, drug effects or as a congenital anomaly. Prolongation of the QT interval is an important predisposing factor for the development of serious arrhythmias.

U Wave

The U wave is an after-potential related to repolarization of either the papillary muscles or the Purkinje network. Generally this has the same direction as the T wave. It is best identified in leads V_3 and V_4.

The ventricular activation time (VAT) denotes the time taken from the onset of the QRS complex to the occurrence of the intrinsicoid deflection (peak of the R wave). It represents the time taken by the impulse to spread from the endocardium to the epicardium and therefore gets prolonged in myocardial hypertrophy or conduction disturbances.

Determination of the Electrical Axis

The electrical axis refers to the mean direction of the vector. Electrical axis in the frontal plane may be calculated for each of the cardiac vectors, viz. the P wave, QRS complex and the T wave. Knowledge of the hexaxial and the triaxial reference frames is critical in understanding axis determination.

These reference frames are simply graphic illustration of the lead systems. Einthoven's triangle formed by leads I, II and III, when rearranged so that the three sides intersect at a common point gives rise to the triaxial reference frame. The hexaxial frame is obtained when the augmented unipolar leads are also introduced into the scheme. Although the axis of the P, QRS and T waves, can all be determined, only the QRS axis is routinely measured (Fig.16.4).

QRS axis anywhere between –30° to +110° may be normal, whereas a mean QRS axis outside this range is usually associated with structural heart disease. If the QRS axis is beyond –30° it is called abnormal left axis deviation. A shift of the QRS axis beyond +110° indicates abnormal right axis deviation. Ventricular hypertrophy, conduction disturbances and myocardial infarction can cause abnormal axis deviations. At birth, since the right ventricle is dominant, the QRS axis is towards the right. With increasing age, the left ventricle becomes larger and the axis drifts leftward.

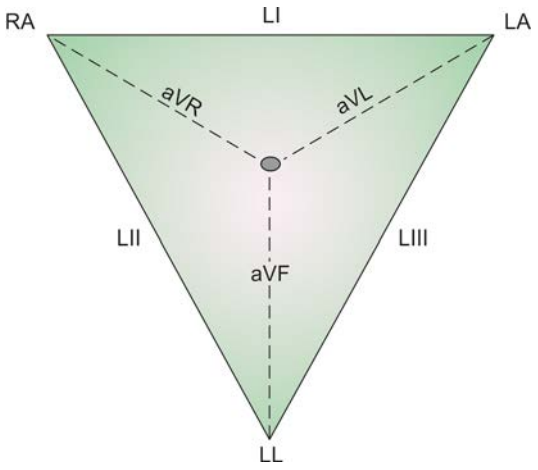


Fig. 16.4: Einthoven's triangle
RA–right arm, LA–left arm, LL–left leg

The reader may consult textbooks on electrocardiography for further details.

General Scheme for the Interpretation of the Electrocardiogram

The following scheme is proposed for the systematic interpretation and reporting of an electrocardiogram.

1. Standardization: normal/half/double
2. Heart rate: Heart rate is calculated by the simple formula:

$$\text{Heart rate} = \frac{1500}{\text{R–R interval in mm}}$$

3. Rhythm
4. P-waves Amplitude, Duration, Axis and Morphology
5. PR interval
6. QRS complex:
 I. Duration
 II. Amplitude of R wave and S wave in different leads, particularly V_1 and V_6
 III. Axis
 IV. Rotation—clockwise or counterclockwise
7. ST segment:
 I. Position—isoelectric, elevated or depressed.
 II. Morphology—upsloping, downsloping, concave, convex, square
 III. Duration
8. T-waves—amplitude, duration, direction
9. U waves
10. QT interval
11. Any other findings
12. Conclusion.

Special Forms of Electrical Recording Signal Averaging Electrocardiography

This refers to the averaging of the root mean square voltages of 100 or more consecutive similar beats so that background activity is masked and repetitive activity is amplified. Currently, this technique has found greatest application in the recognition of ventricular late potentials which may identify a patient at risk of malignant ventricular arrhythmias or sudden death, particularly in the setting of coronary artery disease.

Dynamic (Ambulatory) Electrocardiography (Holter Monitoring)

Routine electrocardiography records the electrical activity during a brief period. However, recording the electrical activity of the heart over extended periods with the patient engaged in all his routine activities is also possible. This technique is referred to as ambulatory electrocardiography or Holter monitoring. This consists of a conventional tape Holter recorder into which all the electrical activities of the entire 24 or 48 hours are recorded. A computer system allows the real time analysis of every beat, along with storage, retrieval, display and print outs of all the data acquired. Modern techniques allow online monitoring, event recording, extended study periods and also trans-telephonic or telemetric transmission of data.

The indications for Holter monitoring are:

1. As a diagnostic tool in the evaluation of symptoms like:
 - Giddiness or syncope
 - Recurrent palpitation
 - Episodic chest pain, dyspnea or fatigue.
2. As a prognostic tool to assess the risk for future cardiac events in the setting of:
 - Coronary artery disease—post MI
 - Hypertrophic cardiomyopathy
 - Congestive cardiac failure
 - Ischemia monitoring—silent, vasospastic or others
 - Arrhythmic potential in Brugada and long QT interval syndrome.
3. In the evaluation of the efficacy of specific therapeutic interventions:
 - Antiarrhythmic drug efficacy
 - Proarrhythmic potential of treatment
 - Assessment of pacemaker and defibrillator function.

Holter study is particularly useful in arrhy-thmia evaluation because it not only documents and quantitates the arrhythmia, but also provides correlation of symptoms to the arrhythmia and also permits evaluation of the efficacy of specific anti-arrhythmic therapy. The precipitating factors, the number and duration of ischemic episodes, and response to antianginal therapy can be documented. *It is with the routine use of Holter monitoring that the concepts of "silent myocardial ischemia" and "total ischemic burden" evolved.*

Exercise Electrocardiography (Syn: Stress Tests, Treadmill Test)

This refers to the recording of the electrical activity of the heart while the individual is subjected to the stress of graded exercises. The bicycle ergometer or the treadmill is currently used for most exercise testing programs. There are various exercise protocols such as the *Bruce protocol* or the *Naughton protocol* to assess effort tolerance. In all these protocols the subject is made to exercise in stages of increasing workloads until the end points are achieved. During exercise, various parameters like occurrence of symptoms, fluctuations in blood pressure changes in the ST segment, and changes in cardiac rate and rhythm are closely monitored. Although the stress test is fairly safe, it has to be done only under close medical supervision.

Currently the main indications for stress testing are:

1. As a diagnostic tool in the evaluation of symptoms like effort induced chest pain, or palpitation.
2. To assess the prognosis and in the risk stratification of patients with coronary artery disease, either after acute events like myocardial infarction or angina, or after therapeutic interventions like coronary angioplasty or by pass surgery.
3. To assess the functional capacity in patients with ischemic heart disease, valvular heart disease, cardiomyopathy and patients undergoing cardiac surgery.
4. As a screening test for ischemic heart disease in subjects with an intermediate or high probability for the disease.

The test is considered positive if there is flat or down sloping ST segment depression of 1 mm or more, ST segment elevation, inversion of U waves, fall in blood pressure and ischemic symptoms associated with ECG changes.

Standard contraindications to exercise testing include acute myocardial infarction, high risk unstable angina pectoris, severe aortic stenosis, congestive cardiac failure, acute pulmonary embolism or infarction, acute myocarditis or pericarditis, aortic dissection, uncontrolled severe systemic hypertension > 200/100 mm Hg, high grade heart blocks, uncontrolled symptomatic cardiac arrhythmias, any acute systemic illness or an unwilling patient.

The indications to terminate exercise testing includes inappropriate drop in blood pressure or deceleration of the heart rate with increasing workload and exercise, moderate to severe angina, sustained VT, ST depression more than 3 mm or ST elevation in non Q leads, hypertensive response > 250/115 mm Hg, patient exhaustion, fatigue, leg cramps or claudication pain and subject's desire to stop the test.

Exercise stress testing has a sensitivity of about 80 to 85% and a specificity of 85 to 90% for the diagnosis of coronary artery disease. *In patients with ischemic heart disease, positive stress test* is *an indication for further tests such as coronary angiography.*

Intracardiac Electrography

This is performed in a cardiac catheterization laboratory. Electrode catheters are introduced transvenously into the right side of the heart. These catheters serve not only to record the intracardiac electrogram, but also permit a variety of stimulation studies, commonly referred to as electrophysiologic testing.

The intracardiac catheters record the electrical activity of the sinus node, His bundle, atria and ventricles. Of crucial importance in arrhythmia analysis is recording the His bundle electrogram. A catheter positioned at the level of the tricuspid valve records His bundle electrogram (H spike) which is characterized by a biphasic or triphasic deflection between the atrial (A) and ventricular (V) electrograms.

Invasive electrophysiological studies help to map out accessory conduction pathways between the atria and ventricles. This is absolutely necessary

for surgical ablation or radiofrequency ablation of these abnormal pathways, which forms the definitive treatment for pre-excitation syndromes and intractable arrhythmias.

ECG Patterns in Health and Disease

Some of the common abnormalities seen in day to day practice and the various conditions for which the ECG is useful, are given in Figs 16.6 to 16.24. Detailed description of the findings is not attempted. The student can appreciate the range of conditions in which ECG provides valuable information for patient care. For individual analysis of the patterns and further description, the student may refer to text books in ECG. A full list of ECG abnormalities is not attempted.

The standard 12-lead ECG consists of 3 standard limb leads, 3 augmented unipolar limb leads and 6 augmented unipolar chest leads.

Normal ECG (Fig. 16.5)

1. In sinus rhythm all QRS complexes are preceded by P waves.
2. PR intervals, QRS complexes, ST segments and T waves are normal in shape and duration.
3. Normal voltages, i.e. QRS exceeds 5 mm in standard leads and 10 mm in some of the precordial leads.

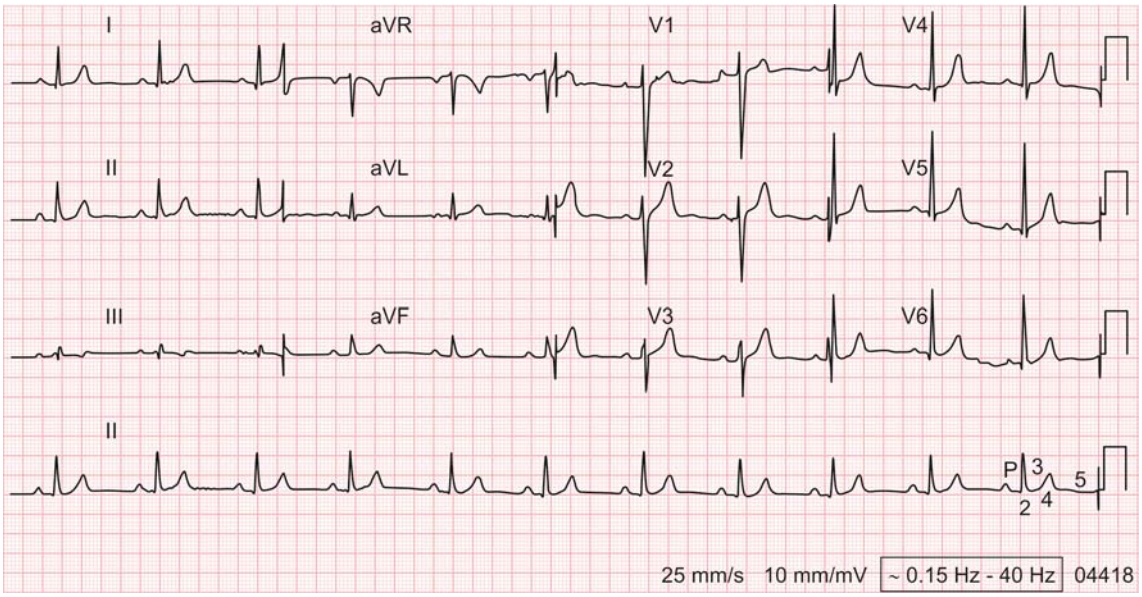


Fig. 16.5: Normal ECG. ECG shows sinus rhythm. Each QRS complex is preceded by a P wave. PR interval in this ECG is 0.16 sec. (Normal PR interval is up to 0.21 sec). QRS duration is also normal, i.e. 0.08 sec (Normal up to 0.1 sec). No ST segment of T wave changes I, II, III, limb leads aVR, aVL, aVF augmented unipolar leads V_1-V_6 unipolar chest leads 2. QRS segment 3. ST segment 4. T wave 5. Position of U wave

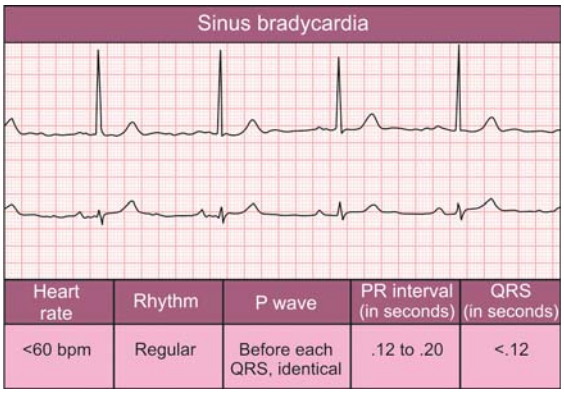


Fig. 16.6: Sinus bradycardia—heart rate < 60 per minute



Fig. 16.7: Sinus arrhythmia—ECG



Fig. 16.8: Sinus tachycardia—ECG



Fig. 16.9: Atrial premature Beats—ECG

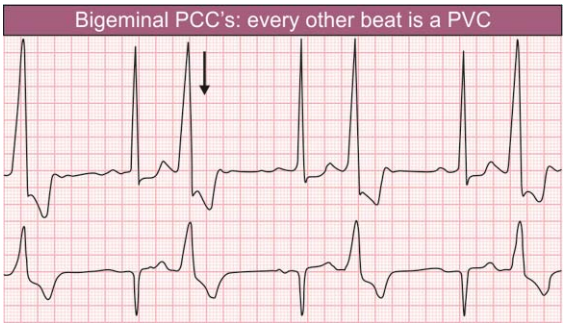


Fig. 16.10: Ventricular premature beats—ECG



Fig. 16.11: Paroxysmal atrial tachycardia—ECG

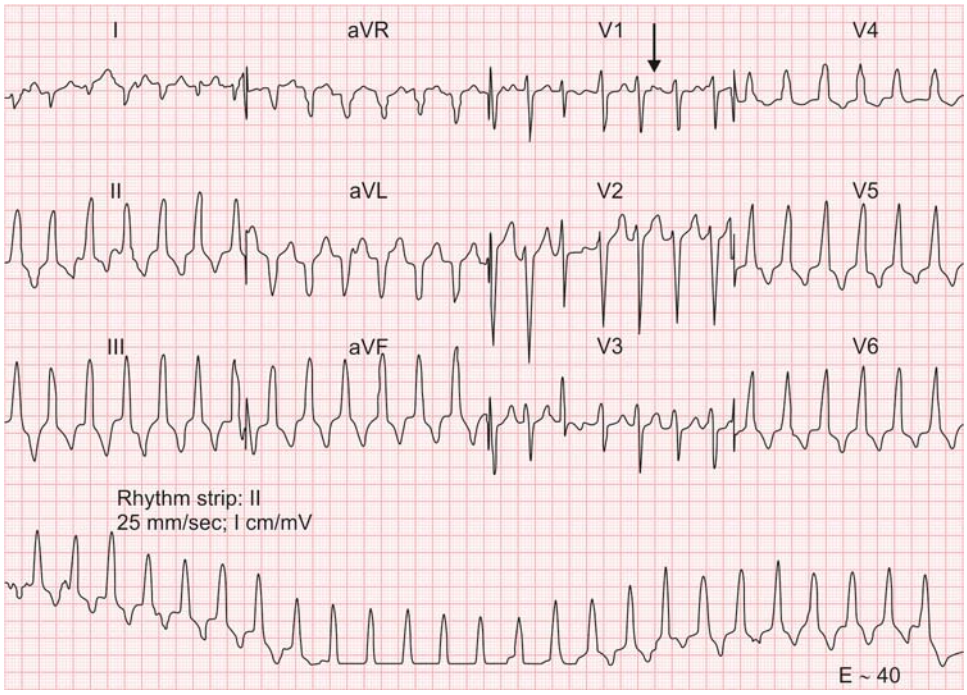
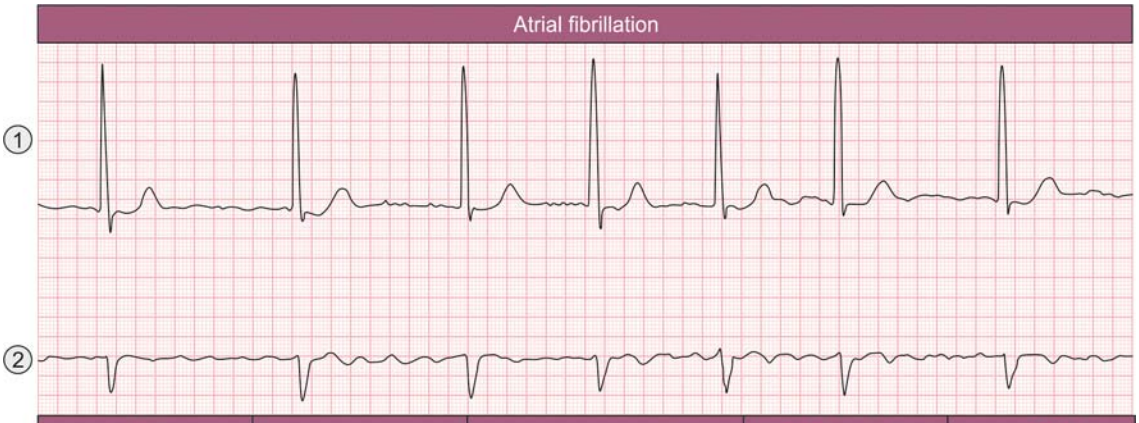


Fig. 16.12: Ventricular tachycardia—ECG



Fig. 16.13: Atrial flutter— ECG



Heart Rate	Rhythm	P Wave	PR interval (in seconds)	QRS (in seconds)
A: 350-650 bpm V: Slow to rapid	Irregular	Fibrillatory (fine to course)	Not applicable	<.12

Fig. 16.14: Atrial fibrillation—ECG

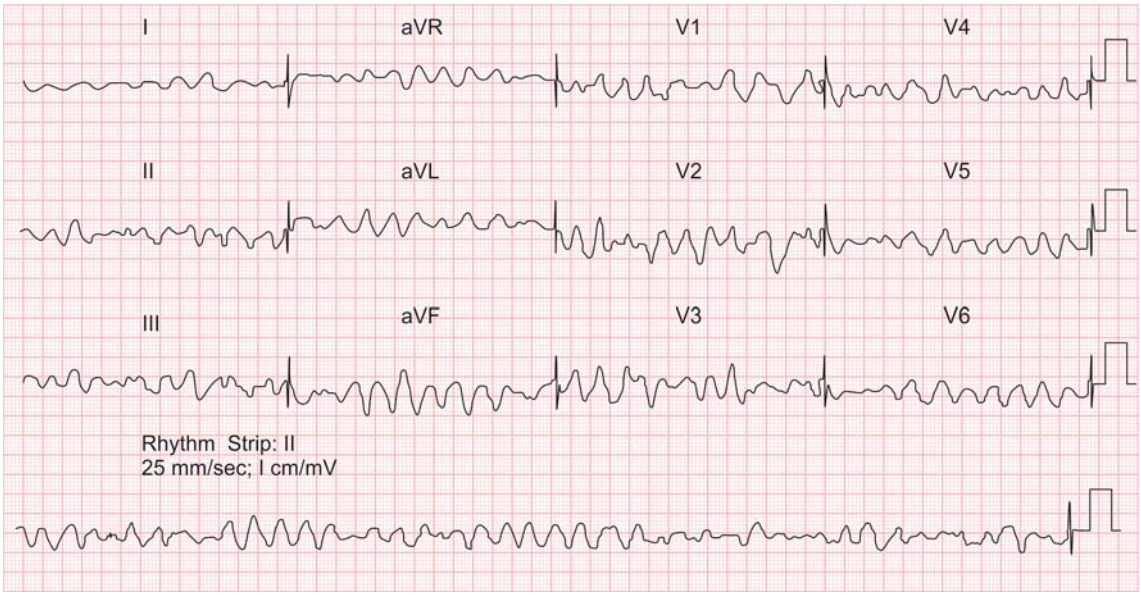


Fig. 16.15: Ventricular fibrillation—ECG



Fig. 16.16: Sinoatrial block—ECG



Fig. 16.17: First degree A-V block—ECG



Fig. 16.18: Second degree A-V block Mobitz type1—ECG



Fig. 16.19: Second degree A-V block Mobitz type 2—ECG



Fig. 16.20: Third degree A-V block—ECG

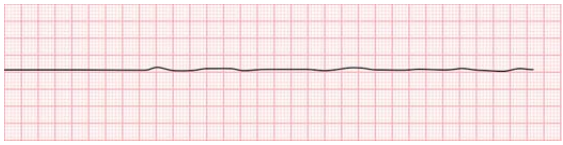


Fig. 16.21: Ventricular–asystole—ECG

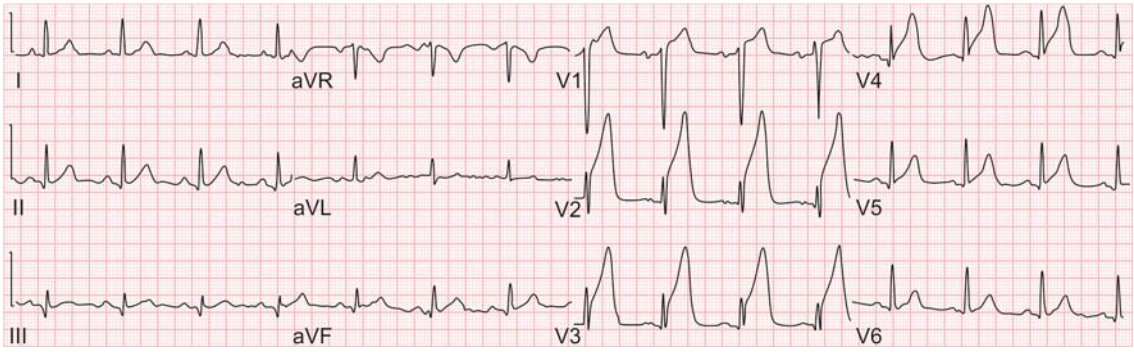


Fig. 16.22: Anterior wall-myocardial infarction (MI)—ECG

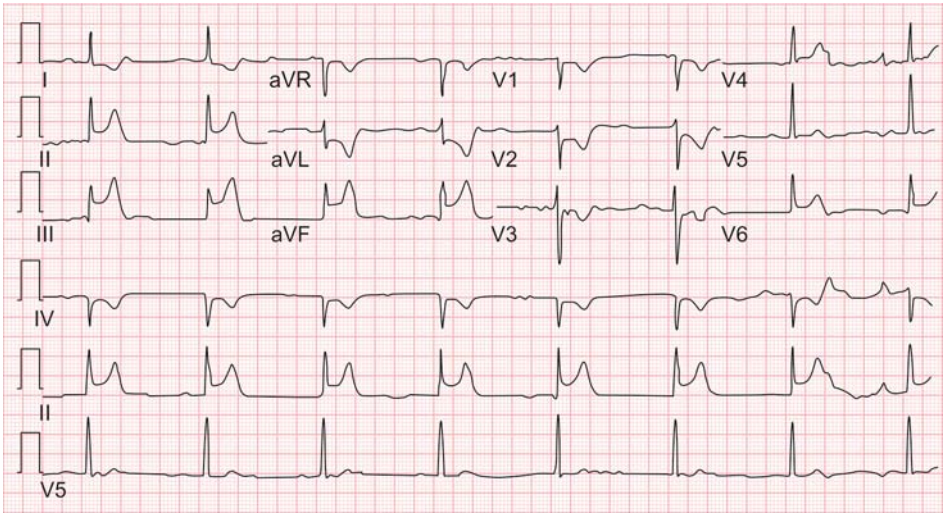
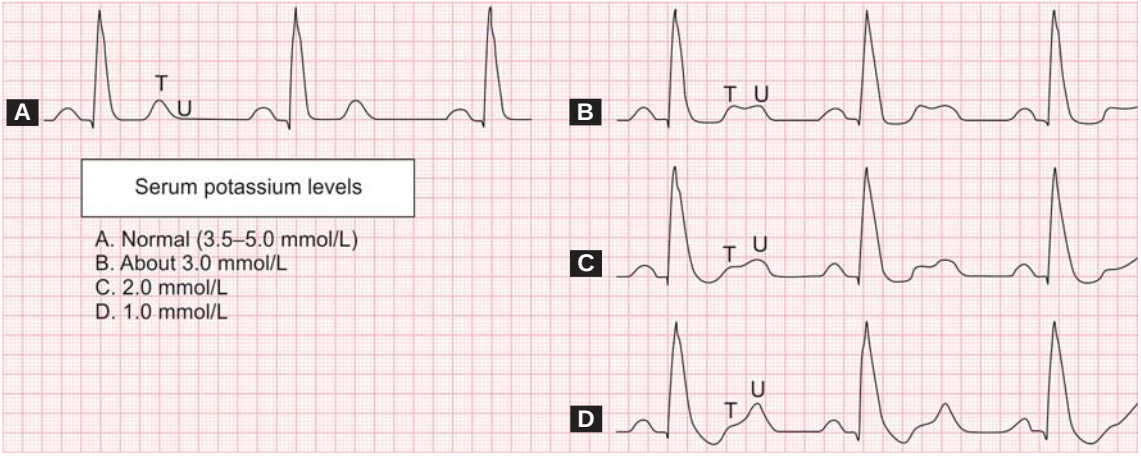


Fig. 16.23: Inferior wall myocardial infarction (IWMI). ST segment elevation in leads II, III and aVF, T wave inversion in leads III and aVF, pathologic Q waves in lead L III and reciprocal ST depression in L1, aVL, V_3,V_4,V_5



Figs 16.24A to D: Hypokalemia—ECG

SYSTEMIC INVESTIGATIONS

Biochemistry, Hemotology, Microbiology, Serology and Routine Urinalysis *(See also Chapter 30)*

Urinary abnormalities may occur in cardiovascular lesions.

Volume of urine: Oliguria is a common accompaniment of all forms of cardiac failure. The urine is concentrated. Nocturnal polyuria occurs during the early stages of development of heart failure. During resolution of edema as a result of therapy, polyuria is the rule.

Abnormal constituents: Mild-to-moderate proteinuria may occur in congestive heart failure even in the absence of intrinsic renal disease.

Microscopic hematuria is a common finding in infective endocarditis. Later there may be findings to suggest glomerulonephritis. Microalbuminuria is an important marker for adverse prognosis in hypertensive subjects.

Hemogram

Erythrocyte sedimentation rate (ESR) is usually around 100 mm/hour in acute rheumatic carditis, active stages of rheumatoid diseases, and systemic lupus erythematosus. Moderate elevation (30-40 mm/hr) occurs in infective endocarditis, pericarditis and acute phase of myocardial infarction.

Anemia

Progressive anemia with hemoglobin levels ranging from 6 to 10 g/dL develops in infective endocarditis. Hemolytic anemia with the presence of fragmented erythrocytes demonstrable in the blood film, occurs rarely as a complication of insertion of prosthetic valves.

Cardiac abnormalities may develop in anemia *per se*. The reduced oxygen carrying capacity of the blood in anemia manifests as fatigue, dyspnea on exertion and angina in patients with coronary artery disease. In all types of severe anemia of gradual onset when the hemoglobin level falls below 7g/dL functional systolic murmurs develop, particularly over the pulmonary and aortic areas. Cardiomegaly and dilatation of the A-V rings may occur.

In secondary polycythemia which occurs in cyanotic congenital heart diseases, packed cell volume is increased above 55% and the erythrocyte count may go above 7 million/cumm. Unlike in polycythemia vera, the granulocytes and platelets do not show proportional increase.

Leukocytes

Moderate neutrophil leukocytosis (TLC 9000–10000 with neutrophils 55–65%) occurs in rheumatic carditis. In subacute bacterial endocarditis the picture is not characteristic, but moderate neutrophil leukocytosis may develop. There may be increase in monocytes. In ulcerative endocarditis caused by pyogenic organisms intense neutrophil leukocytosis may occur (TLC 20000 with neutrophils 80–90%).

Blood Culture

This has to be done to identify the organisms in infective endocarditis. When the lesion is caused by slow-growing organisms of low virulence, special methods have to be employed. Around 5 to 10 mL of venous blood is taken by a fresh venipuncture directly into culture media at hourly intervals for 3 hours and sent to the laboratory for culture under aerobic and anaerobic conditions. The results may be available only after several days. Sometimes blood may have to be cultured on different occasions to get the infective agent. As the bacteremia in infective endocarditis is continous it is not mandatory to send the sample during spikes of fever. Serial blood cultures are done to establish the diagnosis and identify the organism in infective endocarditis. This is necessary since multiple organism may cause infection and therefore the microbial flora may change with progress of the disease.

Biochemical Markers of Cardiac Necrosis

Cardiac enzymes and other components: Normal components of the myocytes get released into circulation when myocardium undergoes necrosis and their serum levels rise. These markers of myocardial necrosis are important both for establishing diagnosis and for predicting prognosis. These investigations are available in even moderate sized hospitals in India.

Indications: Confirm or exclude the diagnosis of acute myocardial infarction.

Quantify the size of infarct and extent of myocardial necrosis.

Assess efficacy of reperfusion induced by thrombolysis or angioplasty.

Risk stratification of patients presenting with unstable angina or acute coronary syndromes.

The commonly used markers of myocardial damage are *aspartate transaminase* (AST) or SOT), *Creatine kinase (CK), CK isoenzymes* (CK–MB), *myoglobin, lactic dehydrogenase* (LDH) and the *cardiac specific troponins*

Aspartate transaminase: Serum glutamic oxaloacetic transaminase (SGOT) levels start rising in 8 to 12 hours, peak at 18 to 36 hours and come down in 3-4 days. Re-infarction causes further rise in SGOT levels. Normal value is up to 40U/L.

Creatine kinase (CK): Levels start to rise within 6 hours of onset of infarction, peak at about 24 hours and come to normal within 48 to 72 hours. Peak levels occur much earlier in patients who have had successful reperfusion. Although very sensitive and widely used, its important limitations are, false positive elevations in patients with skeletal muscle trauma, convulsions, intramuscular injections, diabetes mellitus, alcohol intoxication and others. Normal value is 25 to 195 u/L.

CK isoenzymes—CKMB subfraction: It is a more specific marker for myocardial necrosis. Elevated levels of CKMB, for all practical purposes, indicate myocardial necrosis, usually due to AMI, but also can occur due to myocarditis, DC cardioversion cardiac surgery and others. Normal values is 0.25 u/L.

When levels of the CK and CKMB are twice the upper limit of normal, they are diagnostic of myocardial infarction.

Myoglobin estimation: It is less specific, but levels start rising at (2-4) hours and peak at (6-8) hours, much earlier than *CK*, and returns to normal within 24 hours. Normal value is 25 to 72 ng/mL.

Cardiac specific troponins: The troponin complex, troponin C, troponin 1 (Tn-I) and troponin T (Tn-T) are normal constituents which regulate the calcium mediated contractile process. Quantitative and qualitative methods of assay of cardiac troponins help in the early diagnosis of acute myocardial infarction, especially in those with atypical presentations and doubtful electrocardiograms. They are also useful to detect minor myocardial damage in patients with acute coro-nary syndromes. Cardiac troponins begin to rise within 3 to 6 hours of onset of pain and remain elevated much longer; 7 to 14 days. They are therefore useful even later in the course of illness for diagnosis.

Normal values of troponin T is < 0.01 ng/mL, levels above 0.1 ng/mL are diagnostic. Values between 0.01 and 0.09 ng/mL are doubtful. In such cases the troponin T level should be repeated serially. Elevation of troponins is more specific and reliable in the diagnosis of myocardial infarction.

Serial estimations to document the rise and fall of enzymes are more important than single measurements in the follow-up of cases. Intramuscular injections may cause rise in enzyme levels and therefore blood should be collected before giving IM injections.

Serological Tests (See also Chapter 20)

Antistreptolysin-O (ASO) titer is increased in acute rheumatic fever and rheumatic reactivation. About 2 ml of blood has to be sent without anticoagulant for this test. ASO titres above 200 Todd units in adults and above 333 Todd units in children are suggestive, if other criteria for rheumatic fever are also present. ASO titre can be followed up to assess the progress of the disease.

C-Reactive protein (CRP) is an acute phase reactant derived from the liver. Its role as a minor criterion in the diagnosis of rheumatic fever is well known.

Hs-CRP—High sensitivity C-reactive protein is now being increasingly touted as an independent predictor more reliable than even the LDL-cholesterol levels for future adverse cardiac events. As a marker of inflammation, this helps to identify those patients at higher risk for development of acute coronary syndromes. Hs-CRP levels are increased in patients with diabetes, hypertension, dyslipidemia, obesity, smoking and infections. Hs-CRP levels are reduced by exercise, weight loss, statins, angiotensin blockers and thiozolidinediones. Based on the levels of Hs-CRP low risk is identified as levels below 1 mg/L, high risk as levels above 3 mg/L and intermediate risk at levels between 1 to 3 mg/L.

Hs-CRP measurement is recommended for risk prediction and adoption of lifestyle interventions and appropriate therapeutic strategies in the contexts of both primary and secondary prevention of CAD.

B type or brain natriuretic peptide (BNP) is secreted by the heart and its levels are raised in left

ventricular hypertrophy with or without dysfunction. BNP levels are particularly raised in patients with heart failure and has emerged as a emergency room tool for the quick diagnosis of heart failure in patients presenting with dyspnea. BNP levels are also raised in many conditions which include acute myocardial infarction, high risk unstable angina, acute pulmonary embolism and even in renal failure. A cut off value of BNP below 100 pg/mL (picogram/mL) has a high negative predictive value and a value of over 400 pg/mL has a high positive predictive value for diagnosis of heart failure in patients presenting with dyspnea.

Plasma D-dimer testing is another potential tool and is commonly used in the diagnostic evaluation of deep vein thrombosis and pulmonary embolism. It also is elevated in patients who have acute aortic dissection. It has a great negative predictive value with normal values ruling out the diagnosis.

RADIOLOGICAL INVESTIGATIONS

X-ray of the chest (skiagram) taken in the postero-anterior (PA) view, right and left lateral views and right or left anterior oblique views have been in vogue for over six decades as a reliable, cheap and almost universally available investigation for delineating the major organs of the chest, viz. the heart and great blood vessels, lungs, mediastinal structures, esophagus and the bony skeleton. The X-ray machines available in the earlier part of this century used to take more time for photography and used to deliver higher X-ray exposure to the patients, which by modern standards are unacceptable. Present day X-ray machines are much faster and the dose of radiation delivered to the patient (approximately 30 millirads) is much smaller although still potentially injurious. Plain and contrast radiograph give only still pictures.

Screening procedures employing sophisticated gadgets such as image intensifiers and television screens are widely used for special diagnostic procedures such as angiocardiography and cardiac catheterization and therapeutic procedures such as coronary angioplasty, introduction of stents, balloon mitral valvotomy and others. In such procedures the exposure to ionizing radiations of the patient and doctor and the introduction of fairly large amounts of X-ray contrast media (often iodine containing dyes) into the patient add to the risks of such procedures.

Despite all these limitations, radiography of the chest is a very reliable investigation which is almost universally undertaken. It is available for Rs. 100 to 200 in almost all parts of India (Figs 16.25A to D).

Posteroanterior (PA) view: Patient's chest held in full inspiration is in contact with the X-ray film and the X-ray source is behind by 2 m (Figs 16.25A and B).

Right lateral view: Patient's right axilla is in contact with the X-ray film with the arm held up. X-ray tube is held on the left.

Left lateral view: Patient's left axilla is in contact with the X-ray film, with the hands raised and the X-ray tube is on the right.

Right anterior oblique: 50° to 60° rotation of the patient with the right side of the chest close to the film (Fig. 16.25C).

Left anterior oblique: 50° to 60° rotation of the patient with the left side of the chest close to the film (Fig. 16.25D).

Anteroposterior (AP) view: In this the patient faces the X-ray source and his back is in contact with the film. This is taken when the patient is confined to bed and also when the patient cannot stand up, e.g.- bed X-ray taken in the intensive coronary care setting.

The mediastinal structures appear magnified in this view. The A-P view is also preferred when the structures behind the mediastinum are to be visualized.

The cardiophrenic angles and costophrenic angles are sharp. CTR is the maximum width of heart shadow divided by the width of the thoracic cage from the rib to rib at the level of the right dome of diaphragm Normal cardiothoracic ratio (CTR) is less than 50%. Increase of CTR above 50% suggests cardiomegaly (Fig. 16.25A).

Enlargement of the heart, abnormal contours, presence of calcified shadows in the heart or pericardium and evidence of pulmonary edema should all suggest the possibility of pathological lesions in the cardiovascular and/or respiratory systems.

Plain radiographs of the chest in P A view, right and left lateral views, and oblique views are very useful to determine the cardiac silhouette, cardiothoracic ratio, individual chamber enlarge-

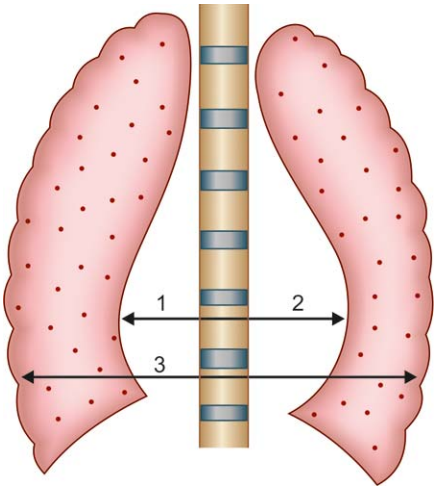


Fig. 16.25A: Normal chest X-ray—PA view diagram (Note 1 + 2 is less than 50% of 3) cardiothoracic ratio (1+2)/3 is less than 50%

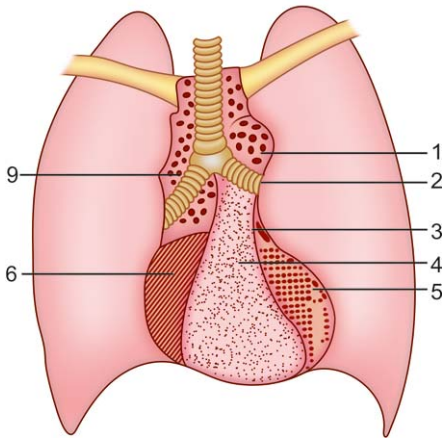


Fig. 16.25B: PA view of the chest diagram

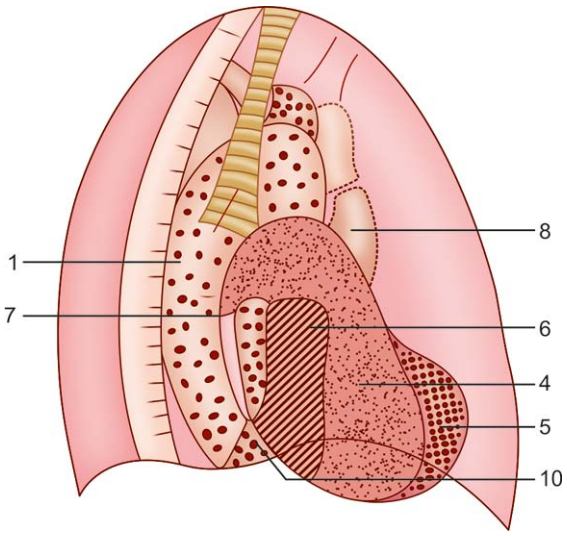


Fig. 16.25C: Right oblique view diagram

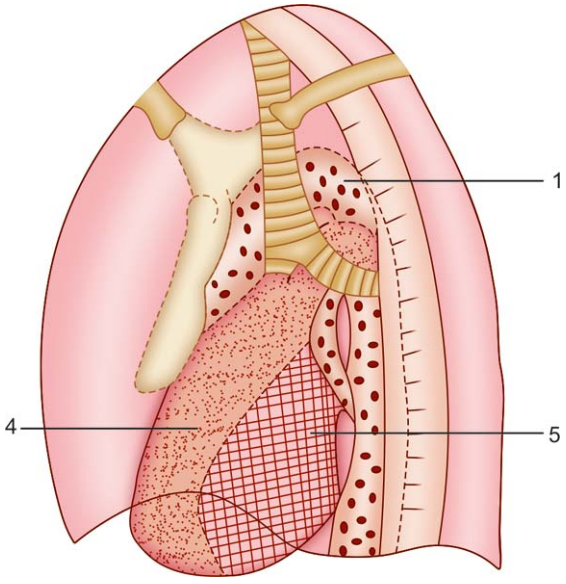


Fig. 16.25D: Left oblique view diagrams
(1) Aorta, (2) Pulmonary artery behind left bronchus, (3) Left artrial appendage, (4) Right ventricle, (5) Left ventricle, (6) Right atrium, (7) Left atrium, (8) Pulmonary conus, (9) Superior vena cava, and (10) inferior vena cava

ment and calcification of aorta and valves. Examination under the fluorescent screen gives information about the movements of the heart chambers and great vessels.

Ventricular enlargement can be demonstrated in lateral chest films. The retrocardiac shadow in front of the vertebral column is obliterated in left ventricular enlargement. In right ventricular enlargement the retrosternal space is encroached upon.

In acute and chronic pulmonary edema caused by left sided heart failure diagnostic information can be obtained. In chronic pulmonary venous hypertension (e.g. mitral stenosis) the presence of dilated lymphatics *(Kerley B lines)* can be seen.

Contrast Radiography

Right anterior oblique view with barium swallow shows the dilated left atrium indenting the esophagus.

Several refinements in radiological techniques give more information, but with the advent of echocardiography, radiological investigations have been superseded to a great extent.

Indications for Skiagram of the Chest

As a regular investigation for health check up. In the case of many silent lesions such as pulmonary tuberculosis, coin shadows in the lungs, hilar shadows, early stages of pulmonary malignancy and others, the abnormal skiagram may be the first evidence of pre-existing disease.

Presence of symptoms such as dyspnea, cyanosis and congestive heart failure and abnormal physical signs such as displacement of the apex beat, presence of abnormal pulsations, presence of adventitious sounds on auscultation, hypertension and others.

For assessing the progress of the disease in acute and chronic cardiovascular diseases, serial skiagrams are very helpful. Some of the abnormal patterns seen commonly are given in Figures 16.26 to 16.31 given, a few common cardiac abnormalities to illustrate the diagnostic help derived from simple radiology. For further details the student may refer to books on cardioradiology.

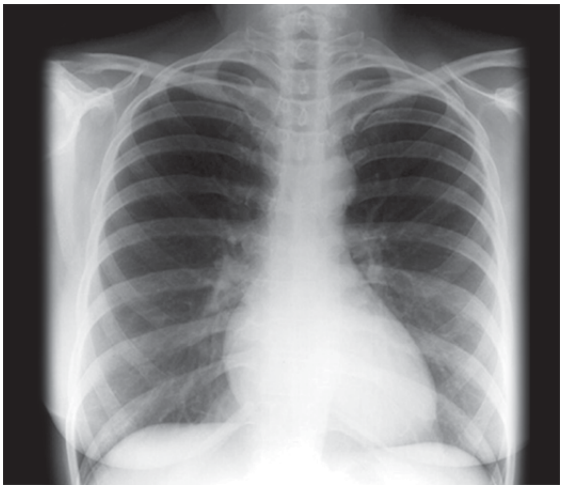


Fig. 16.26: Normal chest X-ray—PA view (refer to 16.25A for details)

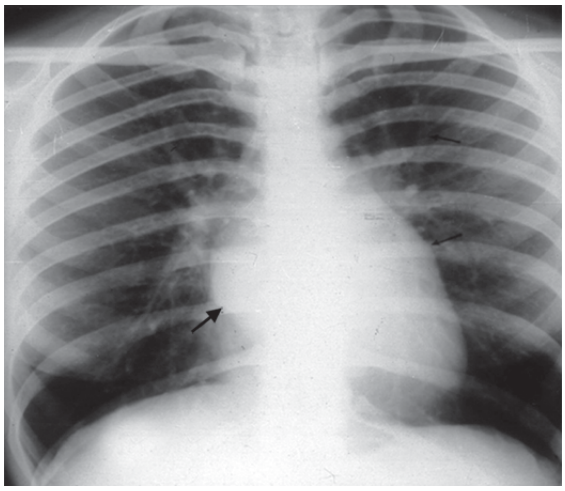


Fig. 16.28: Left artrial enlargement mitral stenosis. *Note:* Enlargement of the left atrium on the right border occupying the middle portion, appearing as double shadow due to overlap on the right atrial shadow (arrow)

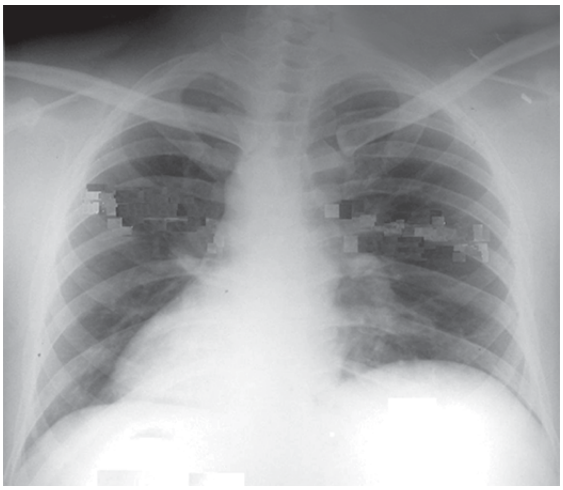


Fig. 16.27: Dextrocardia with situs inversus. The left ventricle is on the right, the liver is on the left causing the left dome on the diaphragm to be at a higher level. Trachea is central

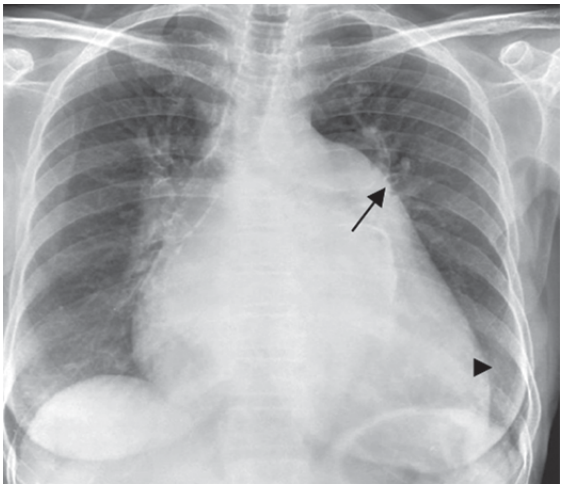


Fig. 16.29: Left atrial enlargement with pulmonary hypertension. Pulmonary artery dilatation in advanced mitral stenosis. *Note:* Left atrial appendage enlargement showing shadow on the left cardiac border (arrow) known as pulmonary conus and also note the contour of the left border in right ventricular enlargement (arrowhead)

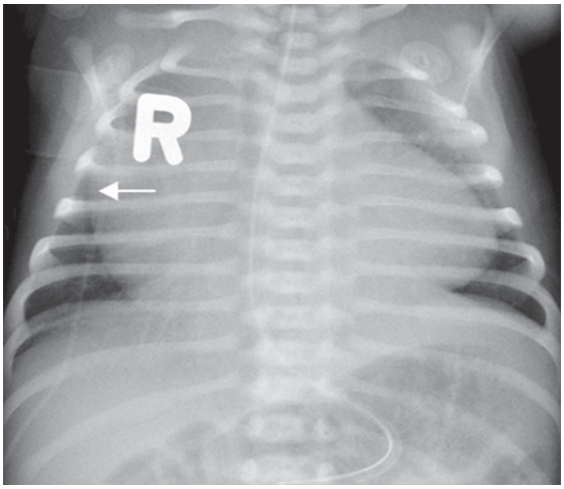


Fig. 16.30: Gross right atrial enlargement. *Note:* the shift of the entire right border laterally – indicating right atrial enlargement (arrow) Ebstein's anomaly

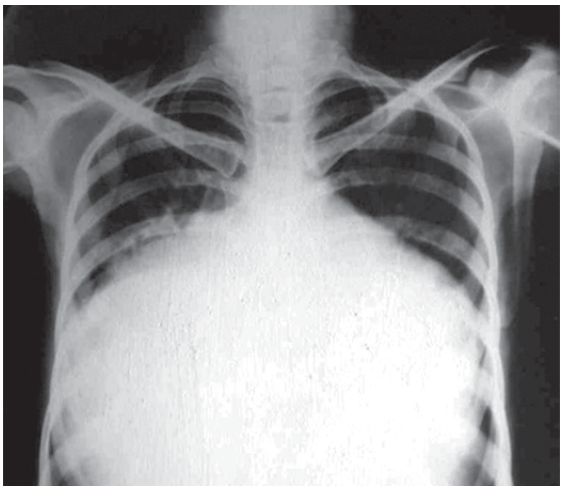


Fig. 16.31: Pericardial effusion. *Note:* gross cardiomegaly, flask-shaped heart, clear lung fields

CARDIAC ULTRASONOGRAPHY (SYN: ECHOCARDIOGRAPHY)

Introduction

The term ultrasound refers to sound waves with frequency above the audible range for human ear, usually greater than 20,000 cycles/second (Hertz—Hz). For medical diagnostic work ultrasound in the mega Hertz range, i.e. over million cycles/ second are employed. Like light, ultrasound can be directed in a beam and it follows the rules of refraction and reflection.

Time motion mode (M-mode), and brightness modulated display mode, (B-mode) are the basic procedures.

The limitation of M-mode study is that structures are depicted along a single dimensional axis as a function of time. In B-mode two-dimensional image is formed and dynamic pictures of the contracting heart can be produced. This is referred to as real time 2D echo.

However developments in cardiac ultrasound have led to many more new applications. These include doppler echocardiography and color flow imaging, tissue doppler imaging, strain imaging, transesophageal echocardiography, contrast studies, and stress echocardiography. Miniature pocket sized portable echocardiographic units are also available today and echocardiography has almost become an extension of the stethoscope.

In contrast-echocardiography: Ultrasound procedures are done after introducing echogenic materials like agitated saline or glucose solution containing echogenic microbubbles which reflect sound. Contrast-echocardiography can be employed to detect shunts and other abnormalities in congenital heart disease. Newer contrast agents for advanced applications help in the delineation of the endo-myocardial border, and assessment of wall motion. Myocardial contrast echocardiography for the study of myocardial viability is another new development.

Doppler echocardiography: registers the shift in frequency of ultrasound directed on to moving objects such as abnormal blood stream. It produces graphic records with a spectral display of velocity plotted against time. Doppler echo studies help to assess hemodynamic significance of valvular lesions and also quantitate shunts.

Color flow imaging: Entails color coding of the Doppler signals to distinguish the velocity and direction of flow. This provides a rapid orientation of the presence and location of lesions like atrial and ventricular septal defects and valvar insufficiency.

Stress echocardiographic imaging: During exercise stress testing or pharmacologic stress testing is another important application of this technique in the evaluation of coronary artery disease (CAD).

Transesophageal echocardiography (TEE): It is performed by using transducers mounted on flexible endoscopes introduced into the esophagus. The advantage is that clear images can be obtained from

close proximity to the heart without inter-position of air in the lungs, and bony cage. TEE is of great use in studying the valves at close quarters, diagnosis of obscure or small cardiac vegetations and other intracardiac abnormalities. It is employed for monitoring cardiac function during surgery and catheter based treatment of valve lesions or septal defects and for the evaluation of prosthetic valves. TEE is invaluable in the identification of structural anomalies like aortic dissection, sizing of septal defects, assessing suitability for device closure and others. It is preferred over transthoracic echo studies in the evaluation of prosthetic valve function and dysfunction especially in diagnosis of prosthetic valve infective endocarditis. Identification of cardiac source for emboli or existence of patent foramen ovale in cryptogenic strokes, are also important new indications for this technique.

Intracardiac echocardiography: Using transducers incorporated into the tips of suitable catheters is also available. So also intravascular ultrasound instruments are available for studying the morphology of atherosclerotic occlusions inside blood vessels. These are employed for assessment of arterial lumen before and after angioplasty (*See* also page 226).

Tissue specific imaging, harmonic contrast imaging, and more recently three dimensional echocardiography are important new developments in this field.

The development and progress in echocardiography have opened out new vistas in the diagnosis of anatomical and functional abnormalities of the heart. The procedure is relatively inexpensive and being totally noninvasive can be universally employed for diagnosis and follow-up of cardiac problems. The outcome of the test and its reliability depend to a great deal on the skill and experience of the person undertaking the procedure.

Fetal echocardiography: It is used for the antenatal diagnosis of congenital heart diseases such as transposition of great vessels; hypoplastic left heart syndrome, tricuspid atresia and others. The transducer is positioned over the mother's abdomen and the study is done in most cases during the 16 to 20th week of gestation. Fetal echocardiography also helps in antenatal treatment of various congenital heart diseases.

Clinical Applications of Echocardiography

1. Evaluation of cardiorespiratory symptoms to detect structural and functional heart disease.
2. Evaluation of cardiac murmurs to ascertain the diagnosis.
3. Diagnostic evaluation and serial follow-up of congenital heart disease.
4. Detection of valvular lesions, quantification of severity, evaluation of changes in symptoms or signs and also for timing of interventions.
5. Diagnosis of known or suspected infective endocarditis.
6. Evaluation of patients with suspected or known ischemic heart disease, detect wall motion abnormalities and to assess left ventricular function.
7. Detection of complications of ischemic heart disease like acute mitral regurgitation, ventricular septal rupture, cardiac rupture, pericarditis, intracardiac thrombi and aneurysm formation.
8. Confirmation of suspected aortic dissection using transesophageal echocardiography.
9. Emergency room echocardiography is useful as diagnostic tool for the evaluation of patients presenting with acute coronary syndromes and nondiagnostic electrocardiogram.
10. For assessment of myocardial diseases like hypertrophic, dilated or restrictive cardiomyopathy, myocarditis and others.
11. To detect left ventricular hypertrophy in patients with hypertension.
12. For quantifying pulmonary artery pressures and assess pulmonary hypertension
13. For detection of pericardial diseases especially pericardial effusion and cardiac tamponade.
14. To detect cardiac masses and tumors.
15. Useful in cases of embolic episodes to rule out a cardiac source of embolism.
16. For evaluation of patients with arrhythmias to rule out underlying structural heart disease.
17. To detect genetically transmitted cardiac diseases such as hypertropic obstructive cardiomyopathy.
18. Evaluation of potential donors for cardiac transplantation.
19. Monitoring of cardiac complications in patients taking cardiotoxic drugs.
20. Stress echocardiography is used for detection ischemia, evaluation of myocardial viability and assessment of valvular lesions.

Note: The expertize in ultrasonography and availability of newer generations of sophisticated machines are opening up newer areas of investigations at a rapid pace.

Figs 16.32 to 16.39 show a few of the common findings obtained by ultrasonography of the heart.

SPECIALIZED INVESTIGATIONS

These are the domain of the cardiologist and these tests have to be undertaken in specialized laboratories. They are all invasive investigations associated with definite, but acceptable risks to health and life.

Coronary Angiography

Coronary angiography (CAG) is used to establish the presence or absence of coronary stenosis, define therapeutic options and determine prognosis in patient with symptoms or signs of ischemic heart disease. (Figs 16.40 and 16.41)

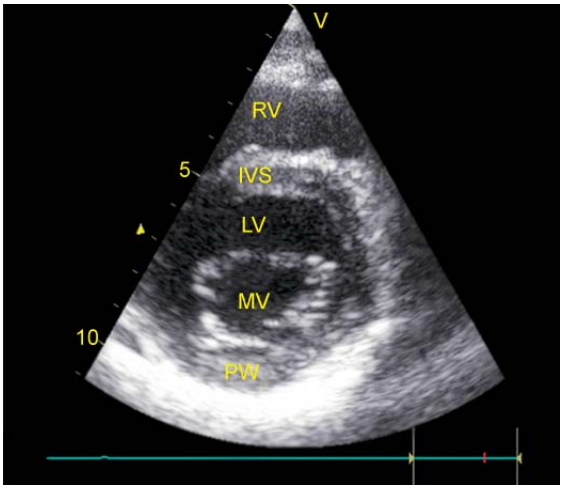


Fig. 16.32: 2D echo—short axis view of the mitral valve level showing the right ventricle anteriorly (RV) mitral orifice (MV) inside the left ventricular (LV) cavity, the interventricular septum (IVS) and posterior wall of LV

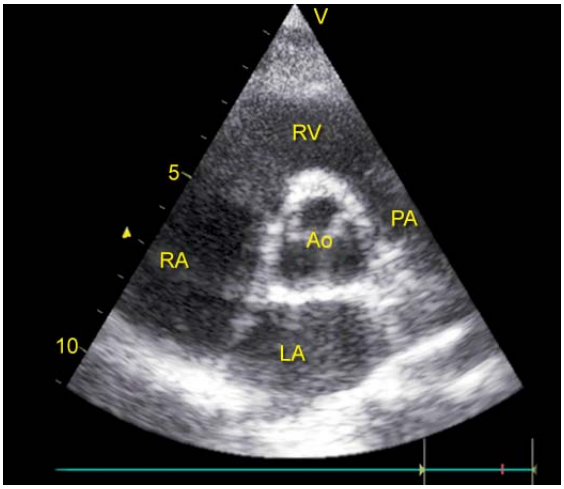


Fig. 16.34: Parasternal short axis view at the outflow level showing aortic valve (Ao) with three cusps, right ventricle (RV) anteriorly and the left atrium (LA) posteriorly

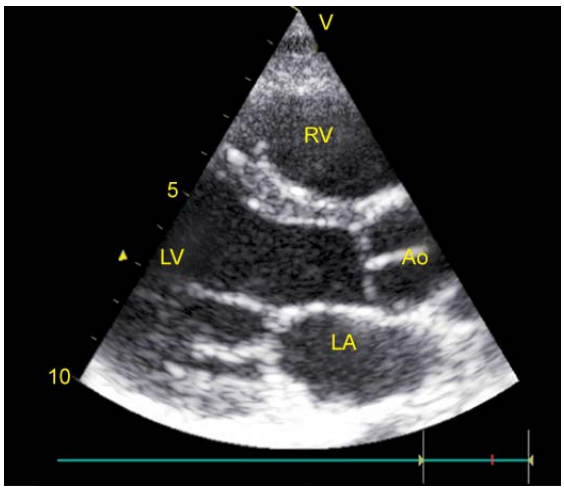


Fig. 16.33: Parasternal long axis view of the heart showing the right ventricle anteriorly (RV), the left ventricle (LV) posteriorly, the left atrium (LA) and the Aorta (Ao)

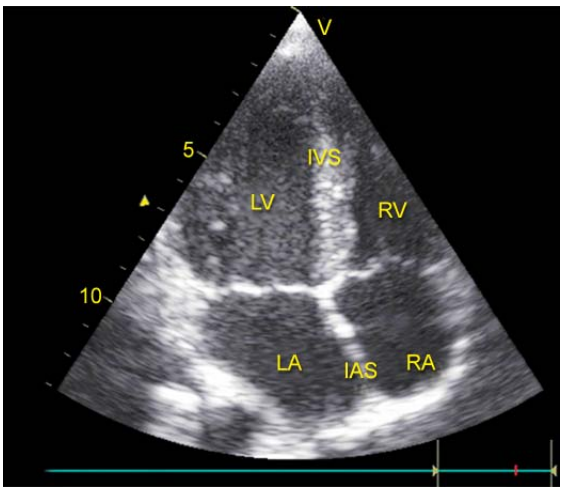


Fig. 16.35: Apical four chamber view of the heart showing the right and left ventricles (RV, LV), right and left atria (RA, LA), interatrial septum (IAS) and the interventricular septum (IVS)

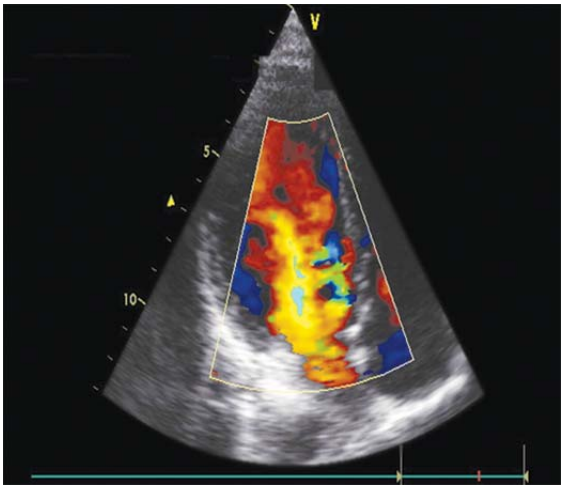


Fig. 16.36: Color flow imaging across the mitral valve. Note the normal diastolic laminar flow into the left ventricle

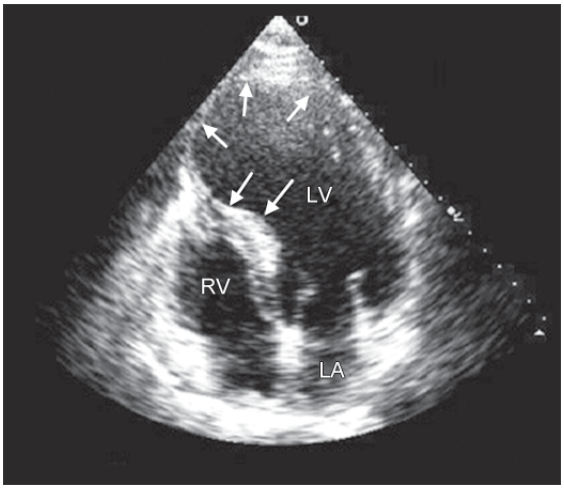


Fig. 16.39: US pictures are reliable to detect morphological abnormalities in cardiac chambers. Arrows delineate aneurysm of the left ventricle (LV)

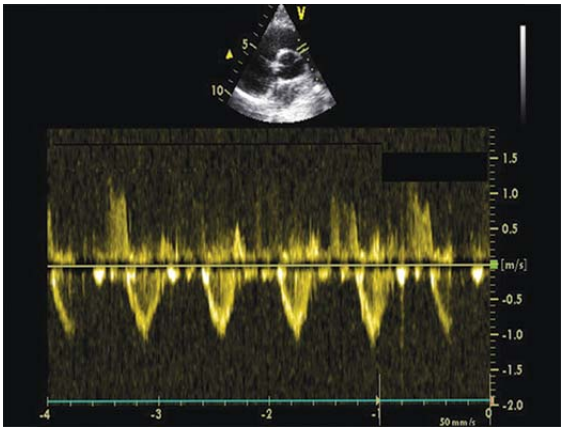


Fig. 16.37: US can be used for studying flow velocities. Note the spectral display of flow velocities across the pulmonary valve in systole

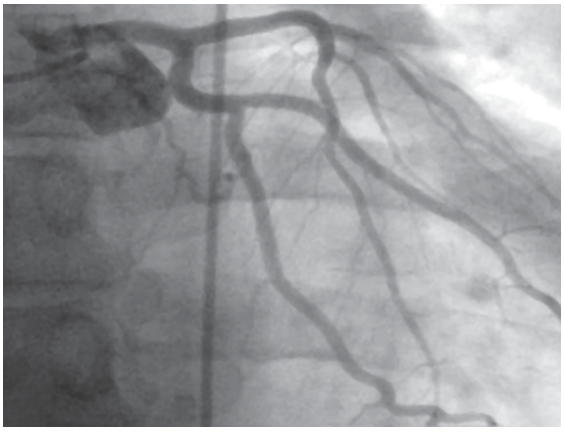


Fig. 16.40: A normal left coronary angiogram showing the left anterior descending artery and the left circumflex artery – the two major branches of the left main coronary artery

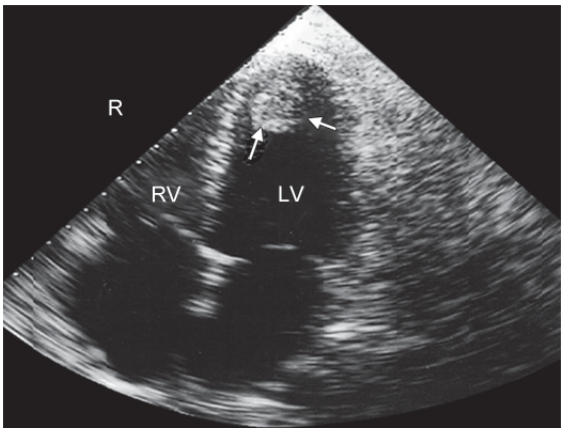


Fig. 16.38: US image detect intracavitary masses reliably. Arrowheads point to mass in the left ventricle



Fig. 16.41: A normal right coronary angiogram showing the entire length of the right coronary artery, its right ventricular branches, posterior descending artery, AV nodal artery and the posterior left ventricular branches

The procedure consists of introducing special catheters through the femoral or radial artery and guiding it up to enter the right or left coronary ostia and in this position injecting radio-opaque dye to obtain imaging of the arteries by rapid sequence photography. The abnormalities of arterial lumen can be demonstrated by this procedure in patients with coronary artery disease. The radial artery approach allows early ambulation after the procedure and less of local complications.

Common indications for coronary angiography (CAG) in different patient groups:

A. Patients with stable angina:
 1. With class III/IV angina despite symptoms, high risk criteria on non-invasive testing or resuscitated from sudden cardiac arrest.
 2. High risk occupations endangering safety of others, e.g. drivers, pilots.
 3. Clinical evidence of heart failure.
 4. Suspected Prinzmetal's angina.

B. High risk unstable angina: Recurrent pain, prior revascularization, arrhythmias, LV dysfunction, Part of early invasive strategy in patients with high risk markers—troponin positive.

C. Patients with acute myocardial infarction:
 1. Prior to primary or rescue angioplasty. Post MI high risk markers—recurrent ischemia, postinfarction angina, LV dysfunction, arrhythmias, hemodynamic instability resistant cardiogenic shock are strong indications.
 2. Patients with post-revascularization symptoms:
 - After CABG—recurrent angina despite optimal medical therapy.
 - After PTCA—suspected acute closure, or stent thrombosis, and recurrent angina, high risk noninvasive markers for ischemia.
 3. Patients with nonspecific chest pain:
 - High risk markers for ischemia.
 - Recurrent hospitalizations.
 - Suspected Syndrome X, Prinzmetal's angina, cocaine use.
 4. Patients with heart failure with chest pain.

D. In patients with valvular heart disease CAG may be required under the following conditions.
 1. In patients above the age of 35, scheduled for valve surgery, to rule out CAD especially if multiple coronary risk factors are present.
 2. If non-invasive testing is equivocal in assessing hemodynamic significance of lesions.

E. Patients before and after noncardiac surgery
 1. High risk criteria on noninvasive testing.
 2. Urgent noncardiac surgery needed after AMI.
 3. Persistent symptoms despite medical therapy.

F. Patients with congenital heart disease
 1. Assessment of hemodynamic impact of congenital coronary lesions
 2. Assess presence of coronary anomalies that could influence surgery
 3. Assess CAD if symptoms or risk factors present

G. Other conditions
 1. Hypertrophic cardiomyopathy with angina or obstruction—if surgery or septal ablation is planned.
 2. Transplant donors/recipients with likelihood for disease.
 3. Before surgery for aortic aneurysms or dissections.
 4. Unexplained cardiac arrest in a young patient.
 5. Kawasaki disease.

In congenital heart disease with possibility of abnormality of the coronary arteries, CAG is done before surgical correction is undertaken.

In aortic diseases like aortic stenosis, income petence, dissection and aneurysm, before surgical correction is attempted. CAG is necessary to assess the vascular status of the myocardium.

Risks and Complications

1. The mortality due to the procedure may go up to 0.1%. Risks are higher in infants and in aged people. Presence of unstable ischemic syndromes, cardiac failure, severe valvular heart disease, severe pulmonary artery hypertension and congenital heart disease increase the risk. Comorbid conditions like renal failure, poorly controlled

diabetes, uncontrolled systemic hypertension, and general debility also increase the risk
2. Exposure to ionizing radiation to the patient and the doctor. This is considerably less in modern machines.
3. Myocardial infarction may develop in 0.07 to 0.6% of cases. Cerebrovascular accidents may develop in 0.03 to 0.2%. Brady or tachy-arrhythmias, especially heart blocks, asystole, ventricular tachycardia, and fibrillation may develop in 0.56 to 1.3%.
4. Local vascular complications at the site of introduction of the catheter may occur in 0.4% of cases. These include vascular occlusion requiring arterial repair, thrombosis, haemorrhage, retroperitoneal bleeding, hematoma formation, pseudoaneurysm, development of arteriovenus fistula and infection.
5. Contrast allergy, anaphylaxis, contrast induced nephropathy and worsening of renal function especially since relatively large quantities of contrast agents are required.
6. Procedure related complications such as aortic dissection, perforation, tamponade, sepsis, hemothorax and others.
7. *Systemic complications:* Mild to severe vasovagal response and cardiac arrest may develop rarely. Other complications include hypotension, cardiac tamponade due to myocardial perforation or coronary laceration, myocardial infarction and acute anaphylactic reaction to the contrast media. Minor complications occur in approximately 4%—commonly transient hypotension and brief episodes of angina.
8. Disruption of the coronary artery and development of myocardial infarction may occur at times. Such patients are taken for emergency coronary artery bypass surgery. Due to this possibility, it is essential that coronary angiography and percutaneous intervention procedures such as angioplasty are undertaken only in centers where cardiac surgical support is available.

Intravascular Ultrasound

The state of the interior of the lumen of the coronary arteries can be studied ultrasonographically by using ultrasound devices mounted on special catheters. Intravascular ultrasound (IVUS) study is particularly useful for the study of the details of plaque characteristics and also in interventional cardiology after angioplasty to study the apposition of stent to the vessel wall. It is also of value in tissue characterization in the vessel wall (*See* also page 219).

COMPUTED TOMOGRAPHY

Computed tomography of the heart usually requires modification of the standard CT techniques. Currently spiral and multi-array CT scanners with exposure times of less than 1 second are available for evaluation of lesions of the thoracic aorta, pericardial disease, paracardiac and intracardiac tumors and patency of coronary arterial bypass grafts. For the assessment of cardiac dimensions and function in addition to morphology, millisecond CT scanners are required. *Electron beam CT scanner* (EBCT, Ultrafast CT) employs a focused X-ray beam that provides complete cardiac imaging in 50 ms. It can be used to assess global and regional myocardical function. Nearly always intravenous injection of iodinated contrast medium is used to delienate the blood pool on CT scans.

The CT has the capability of identifying not only the endocardial wall but also the epicardial surface. Wall thickness and myocardial mass have been estimated accurately with EBCT. The CT can be used in the assessment of the dynamics of regional myocardial wall thickening. It also provides a measurement of total ventricular stroke volume. After myocardial infarction, CT can be used to demonstrate regional wall thinning and complications of infarction such as left ventricular aneurysm and mural thrombus. EBCT may also be able to provide an indication of regional myocardial perfusion. EBCT has been used in the past few years for the detection of calcification in the coronary arteries which may be associated with atherosclerosis.

The CT provides distinct visualization of the pericardium. It is very useful for the diagnosis of pericardial diseases like congenital anomalies of pericardium, pericardial effusion, constrictive pericarditis, pericardial masses and others. Standard CT and EBCT are very useful in the diagnosis of congenital heart disease, thoracic aortic aneurysm, aortic dissection, intramural hematoma and atherosclerotic ulcerating plaque. EBCT and spiral CT have also been used for establishing or excluding a diagnosis of pulmonary embolism.

Multislice CT Coronary Angiography

Modern CT scanners permit the acquisition of multislice-64, 128, or 256-images of the coronaries and image reconstruction algorithms with electrocardiographic gating allow the synchronization of these images to the cardiac cycle and provide virtually artefact free imaging of the entire coronary tree. Contrast enhanced imaging gives a nearly reliable visualization of coronary vasculature, but this technique has not yet replaced the conventional invasive coronary angiogram. While the EBCT has greater value in the detection of coronary calcium, mutlislice CT coronary angiography is a valuable noninvasive tool for the visualization of the coronary lumen. The need for use of contrast agents and the radiation exposure in MDCT is however more than that for conventional invasive coronary angiography.

Indications for Multislice CT

1. For evaluation of symptomatic patients with intermediate risk for CAD.
2. Clinical triage of the patients with acute chest pain syndrome—triple rule out (CAD/Aortic dissection/Pulmonary embolism).
3. Detection of vulnerable plaque.
4. Evaluation of coronary stents—has high negative predictive value.
5. Graft study.

MAGNETIC RESONANCE IMAGING

In the earlier stages of development of magnetic resonance imaging (MRI) it was used primarily for the demonstration of structural lesions. At present MRI is used for the quantification of global and regional ventricular functions, for quantification of valvular heart disease, for the measurement of blood flow in the heart and great arteries and for the assessment of myocardial perfusion and coronary blood flow as well.

Ischemic heart disease. *ECG gated spin echo and cine MRI techniques* permit determination of wall thinning and detection of complications like ventricular aneurysms. It can also quantify segmental myocardial function. Regional myocardial ischemia can be demonstrated by stress testing along with the imaging. MRI can be used to measure coronary blood flow at rest and during interventions intended to test coronary flow reserve.

Diseases of the myocardium, and pericardium and cardiac chambers—MRI provides direct visualization of the myocardium with excellent delineation of the epicardial and endocardial surfaces. It is useful in the diagnosis of cardiomyopathies. Pericardial diseases are well demonstrated. MRI is very useful to demonstrate intracardiac and paracardiac masses.

MRI can be used to identify the presence of valvular stenosis and regurgitation. This is done using cine MRI techniques.

Congenital Heart Disease

MRI also has multiple capabilities for evaluation of congenital heart disease. Morphological information is provided by ECG-gated spinecho and cine MRI. Ventricular volumes, mass and function can be obtained using cine MRI. Visceroatrial situs, the type of ventricular loop and the relationship of great vessels can be identified.

Diseases of the Aorta

MRI is an extremely important investigation in the diagnosis and monitoring of aortic diseases such as aortic aneurysms, and dissection.

NUCLEAR IMAGING

Nuclear cardiology has a decisive role in the noninvasive detection of CAD, assessment of myocardial viability and risk stratification. The regional distribution of coronary myocardial perfusion can be visualized with radiopharma-ceuticals that accumulate proportional to regional myocardial flow. The common agents used are Thallium^{201} and ^{99m}Technetium sestamibi. These radionuclide tracers are injected into the blood stream and they are taken up by the myocardium according to its distribution of blood supply. They emit gamma rays which are detected by means of special gamma cameras.

Both hot spot imaging and cold spot imaging are commonly used techniques in evaluation of CAD. Two types of imaging are common—planar imaging and the more complex SPECT *(single photon emission computed tomography).*

The clinically most important application of myocardial perfusion imaging is in conjunction with stress testing for evaluation of ischemic heart disease. Thallium^{201} and Technetium^{99} are the commonly used tracers and in conjunction with stress

protocols like exercise or pharmacological agents like adenosine, dipyridamol, or dobutamine can detect ischemia and myocardial viability. Radioisotope is injected during stress and images are obtained during stress and rest.

After Th^{201} injection initial uptake depends on the coronary flow hence it is less in areas supplied by diseased coronary vessels. During redistribution phase differential washout occurs which results in reversible filling defect which indicates ischemic but viable myocardium. A persistent filling defect indicates infarcted nonviable myocardium. Extent and severity of the perfusion abnormality are independently associated with clinical outcomes.

The technique of radionuclide angiocardiography allows for evaluation of ventricular function and to some extent allows detection of structural heart disease. This method helps to detect regurgitant lesions and left to right shunts, though it is inferior to standard echocardiographic examination in this respect. But it is the gold standard for the quantitative assessment of ventricular function at rest and during exercise (Fig. 16.42).

There are two types of radionuclide angiocardiograms:

1. First pass radionuclide angiocardiogram (FP-RNA).
2. Equilibrium radionuclide angiocardiogram (ERNA).

POSITRON EMISSION TOMOGRAPHY

Positron emission tomography (PET) is another nuclear cardiology technique which is unique in its ability to image and quantify metabolic processes and blood flow. It is the gold standard for detection of myocardial viability in ischemic heart disease. The PET uses positron emitting radionuclides like F^{18} and N^{13}. Basically the available radiotracers are of two types—those that evaluate myocardial perfusion and those that evaluate myocardial metabolism. They are labeled with other molecules to form compounds like rubidium^{82}, N^{13} ammonia which are perfusion tracers and F^{18}DG (F^{18}- fluoro-2-deoxy glucose which is a myocardial metabolic tracer. The disadvantages with PET are its limited availability, need for on-site cyclotron, short half life of tracers, and the high costs.

CARDIAC CATHETERIZATION (FIG. 16.42)

Introduction of specially designed catheters through the femoral vein cephalic vein, branchial artery or femoral artery into the central parts of the circulation and into individual chambers is a commonly undertaken investigation in cardiology

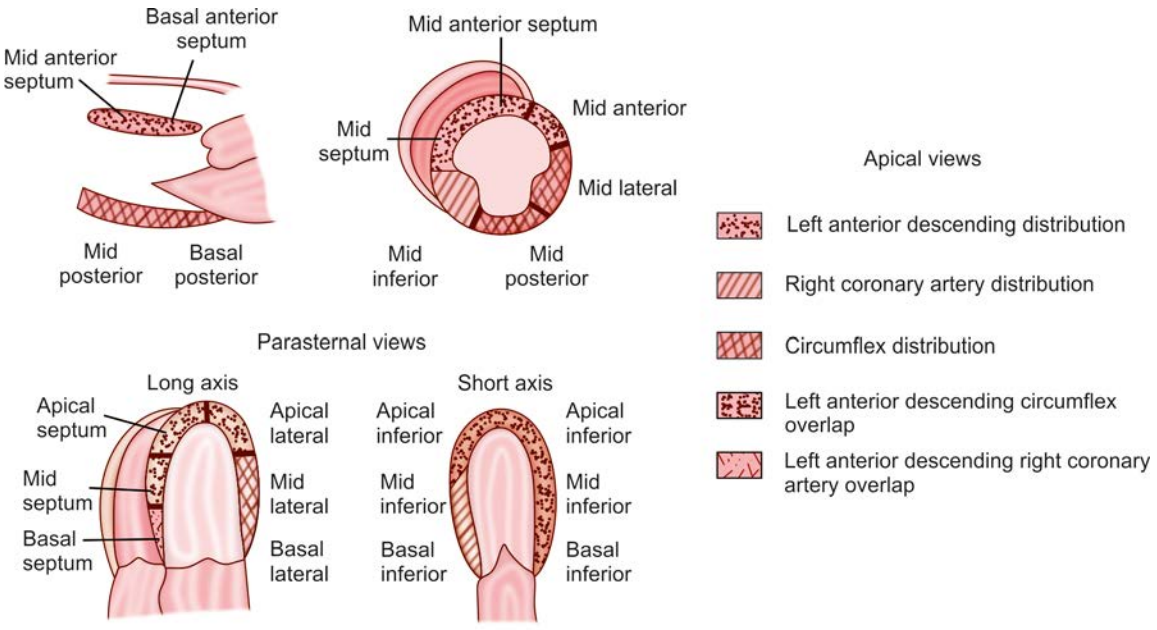


Fig. 16.42: Segment division of left ventricle and the associated coronary artery distribution

centres. Through the venous system the right sided chambers can be entered, and the catheter tip can be further advanced into the small pulmonary arteries and wedged. Events in the right atrium, right ventricle and pulmonary arterial circulation can be studied.

Through the arterial system the left ventricle can be entered. Events in the aorta and left sided chambers can be studied. The studies undertaken by catheterization include recording of pressure in individual chambers and major vessels, pulmonary wedge pressure (which represents the pulmonary venous pressure), sampling blood for its oxygen content (oxymetry) and injection of dye into different areas in the heart and vessels to study its anatomy angiography. By suitable manipulation of the catheter tip, presence of shunt lesions can be demonstrated. Digital subtraction angiography improves the quality of the pictures and the safety of the procedure.

Cardiac catheterization is no longer just an investigatory tool. Several modifications and improvements in this basic technique have taken place. These include interventions such as mitral and aortic valvotomy, septostomies (puncturing the interatrial septum to make an artificial communication), coronary artery angiography, coronary artery dilatation and scaning (angioplasty), atherectomies and others. Using suitable bioptomes, biopsies can be taken from different portions of the endocardium and subjacent muscle. Defects can be closed by catheter based techniques using various kinds of coils or other devices (*See also page 223*).

CHAPTER

17 Cardiac Arrest and its Management

K Suresh, KV Krishna Das

Basic life support measures, Advanced life support care, External defribrillation

Cardiac arrest is defined as abrupt cessation of cardiac pump function, which may be reversible but will lead to death in the absence of prompt intervention.

Suspect cardiac arrest when there is sudden collapse in any subject. Confirm cardiac arrest by:

a. Absence of pulses,
b. Absence of heart sounds and
c. Absence of respiratory movements.

BASIC LIFE SUPPORT MEASURES

High quality cardiopulmonary resuscitation (CPR) improves victims' chances of survival. Institute CPR (*basic life support activities*) immediately.

1. Place the subject supine on a hard surface and loosen all clothing.
2. Deliver a sharp blow over the front of chest on the lower third of the sternum *(precordial thump version)*. In a few cases, this may start off effective cardiac contractions.
3. The new recommendations place emphasis on change from the ABC to the CAB sequence, viz. Chest compressions first, then clear airways and third is breathing.
4. External cardiac massage: Place the palm of one hand over the lower end of the sternum and the other hand firmly over the dorsum (Fig. 17.1). Depress the sternum approximately 3 to 5 cm with sufficient force to generate a palpable pulse. The rate of compressions should be at least 100/minute. After each compression allow chest to expand completely.



Fig. 17.1: External cardiac massage procedure

5. Next is to clear the airway and establish effective ventilation:
 i. Tilt the head backwards, lift the chin, remove foreign bodies from the mouth and throat manually (Fig. 17.2).
 ii. *Heimlich maneuver:* Deliver a sharp blow or compressive movement to the upper abdomen with the closed fists. This may dislodge any foreign body impacted in the throat.
 iii. Turn the patient to one side and deliver 3 to 4 sharp blows over the back between the shoulder blades with the heel of the hand to dislodge foreign bodies from the airways.
 iv. Mouth to mouth respiration should be started and continued until better respiratory assistance is available, either in an emergency ambulance or in the hospital.

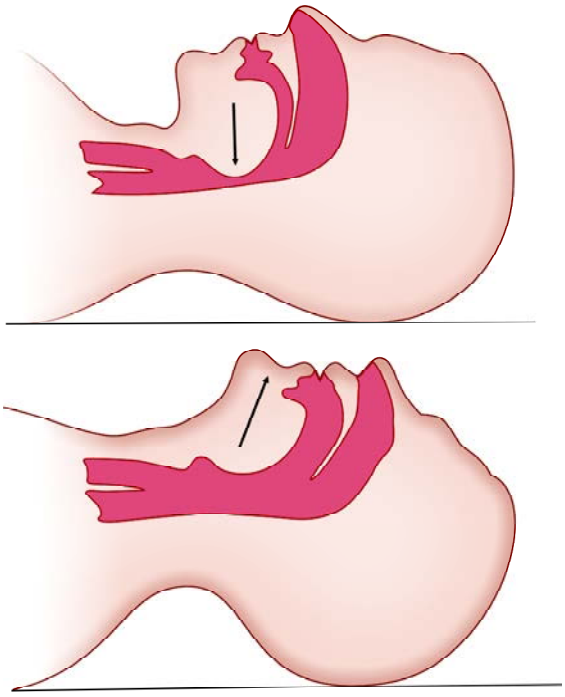


Fig. 17.2: Patency of airway in different positions of the head

Procedure: Pinch the nose, and with your mouth applied to the patient's mouth, breath forcibly out into the patients mouth, using the force generated by your cheek muscles, expiration occurs passively. 10 to 15 respirations should be given every minute by one member of the team.

For adults attended to by two rescuers, a compression-ventilation ratio of 30:2 is now recommended. For two-rescuer CPR for infants and children, the recommended compression-ventilation ratio is 15:2. Once ventilation and effective cardiac massage are established, arrange for the ambulance to transport the patient to a cardiac intensive care room in a hospital. Further steps in cardiopulmonary resuscitation will depend upon rapid transportation of the patient to a hospital for advanced life support care.

ADVANCED LIFE SUPPORT CARE

The basic life support activities are continued till the patient is moved on to more efficient and organized line of management. Advanced life support care in the resuscitative sequence is designed to achieve definitive stabilization of the patient.



Fig. 17.3: Cardiac defibrillation procedure. *Note:* Placement of electrodes

Advance airway management and supplemental oxygen use is part of ACLS.

Respiratory Assistance

Endotracheal intubation is carried out and assisted ventilation is instituted using pure oxygen or oxygen enriched air. Till mechanical ventilation is established, an Ambu bag may be used with a tight fitting facial mask to give effective ventilation.

Cardiac Resuscitation

Monitoring of the cardiac rhythm (to distinguish between ventricular fibrillation and asystole) is established by connecting the patient to cardiac monitor defibrillator and observing the electrical activity on the monitor (Fig. 17.3). Definitive management for the specific cardiac rhythm abnormality is then planned.

Procedure

Rhythm is ventricular fibrillation (VF) or ventricular tachycardia (VT)

1. An initial shock of 360 J should be delivered by devices delivering monophasic waveforms and 120 to 200 J using biphasic devices. Failure of the initial shock to provide an effective rhythm is a poor prognostic sign. Failure of a single adequate shock to restore a pulse should be followed by continued CPR and a second shock delivered after five cycles of CPR.
2. Establish an intravenous drip with normal saline.
3. If VT or VF still persists, epinephrine 1mg IV is administered and followed by repeated defibrillation attempts at 360 J (monophasic) or 200 J or more (biphasic). Epinephrine may be

repeated at 3 to 5 minute intervals with a defibrillator shock in between. Vasopressin (40 units IV single dose) has been suggested as an alternative to epinephrine.

4. For the patient, who continues to have persistent or recurrent VT or VF despite DC cardioversion after epinephrine, electrical stability of the heart may be achieved by intravenous administration of antiarrhythmic agents during continued resuscitation efforts. Intravenous amiodarone bolus (150 mg over 10 min) is the initial drug of choice.
5. A bolus of lidocaine (1.5 mg/kg) may be given intravenously and the dose repeated in 2 minutes for patients in whom amiodarone is unsuccessful and possibly for those who have an acute transmural myocardial infarction as the triggering mechanism for the cardiac arrest.
6. For patients in whom acute hyperkalemia is the triggering event for resistant VF or who have hypocalcemia or are toxic from Ca^{2+} entry blocking drugs, 10% calcium gluconate may be helpful.
7. Some resistant forms of polymorphic VT or torsades de pointes, rapid monomorphic VT, ventricular flutter (rate $\geq$ 60/min), or resistant VF may respond to intravenous beta blocker therapy or IV $MgSO_4$ loading does of 1 to 2 g IV in 10 mL of 5% dextrose over 10 minutes. Magnesium is a drug to prevent or treat recurrent or persistent VT.

Asystolic Arrest and Pulseless Electrical Activity

1. Reconfirm the rhythm at least in two leads
2. Maintain continuous CPR
3. Administer adrenaline in a dose of 1 mg IV. If the intravenous route fails to elicit electrical activity of the heart, these drugs can be given intracardiac into the right ventricular cavity through a 10 cm long needle introduced through the left third intercostal space close to the sternum. Presence of the needle tip in the ventricular cavity can be confirmed by withdrawing blood into the syringe.
4. Identify and treat reversible causes. These include hypovolemia, hypoxia, hypothermia, hypo or hyperkalemia, hydrogen ions, cardiac tamponade, tension pneumothorax, thrombosis, toxins, preexisting acidosis, drug overdose, and others.
 Cardiac pacing: If the asystole continues, external cardiac pacing used to be recommended. However current guidelines do not recommend routine external transcutaneous pacing for asystole or PEA. Pacing is reserved for patients with hemodynamically unstable bradycardias. External cardiac pacing using trans thoracic paddles over the back and precordium may be life saving in such situations where intensive care facilities are not available for insertion of transvenous temporary pacing leads into the right ventricle.

When to Abandon the Attempt for CPR?

If after 15 to 20 minutes of CPR, there is no organized ventricular electrical activity and no effective systemic perfusion as indicated by deep unconsciousness, absence of respiration and dilated-fixed pupils, CPR may be discontinued. However, in hypothermia and poisoning by barbiturates and other narcotic poisons recovery has occurred even after hours of cardiac arrest and therefore, the general guidelines may have to be modified, and CPR continued for much longer periods.

ELECTRICAL CARDIOVERSION

The terms cardioversion and defibrillation need to be clearly understood.

Cardioversion is defined as delivery of energy synchronized to be QRS complex, while random delivery of high energy shock not synchronized to the QRS complex is termed defibrillation.

Defibrillation is employed in a cardiac arrest situation as part of BLS or ACLS measures. Cardioversion simply means termination of tachyarrhythmias, and can be by pharmacologic means or by electrical shock. Electrical cardioversion is done in many conditions where rapid termination of an arrhythmia is warranted.

Indications

1. As a life saving measure, to terminate ventricular fibrillation or ventricular tachyarrhythmias.
2. As an emergency treatment for immediate control of heart rate in supraventricular arrhythmias like atrial fibrillation, atrial flutter or atrial tachycardia, particularly when associated with acute myocardial infarction, cardiogenic shock or pulmonary edema.
3. As a procedure for elective conversion of chronic arrhythmias like atrial fibrillation, flutter or atrial tachycardia to sinus rhythm.

Contraindications

- Tachycardias associated with increased automaticity (multifocal atrial tachycardia and junctional tachycardia)
- Sick sinus syndrome
- Toxicity to digitalis in patients on chronic digoxin treatment
- Hypokalemia.

Complications

1. Thromboembolism, particularly cerebral embolism after conversion of atrial fibrillation to sinus rhythm.
2. Progressive myocardial damage due to intense or repeated electric shock.
3. Ventricular tachyarrhythmias may be precipitated by DC shock, especially in digitalized patients.
4. Atrial tachyarrhythmias may be produced by DC shock. However, these respond to additional DC shocks in most cases.
5. Bradyarrhythmias may develop and stable sinus rhythm may not follow. This may indicate sick sinus syndrome.
6. Superficial skin burns may develop under the defibrillator electrodes.
7. Injuries to operator.
8. Trauma to chest wall, including rib fracture.

SECTION

7

Musculoskeletal and Locomotor System

CHAPTER

18 Rheumatology

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General considerations, Disease pattern affecting the locomotor system in India

GENERAL CONSIDERATIONS

Diseases of musculoskeletal system are among most common of human afflictions. Their prevalence is highest among elderly but these conditions affect all age groups and are associated with disability, impairements, handicaps and job loss.

Rheumatology is that branch of medicine concerned with disorders of the musculoskeletal or locomotor system including inflammatory and other joint diseases, generalized connective tissue disorders, back problems and disorders of periarticular tissues (WHO).

The targets of a proper rheumatological examination are the axial and appendicular musculoskeletal system and the related connective tissues of the body.

Bones

The human body has about 206 bones. Structurally, they can be divided into spongy and compact bones. In spongy bone, the lamellae are stacked one above the other as trabeculae. In compact bone, the lamellae are arranged closely in concentric circles around a central canal containing the osteocyte. Spongy bones house the bone marrow whereas compact bones do not. During bone formation and repair different cells such as osteocytes, osteoblasts and osteoclasts act in a coordinated and orderly manner under the influence of several humoral factors. Bone turn over is mediated by a balance between bone forming cellular activity of osteoblasts and the bone resorbing osteoclasts. Periosteum covers the bone which has an inner cellular layer and an outer fibrous layer which merges gradually into the surrounding muscle.

Long bones transmit body weight and act as levers for movement. The middle part of the tubular shaft is the diaphysis which is flanked on either end by the metaphyseal regions. The ends are expanded to form the articular areas, the epiphyses. Long bones derive their blood supply from diaphyseal, metaphyseal, epiphyseal and periosteal nutrient arteries. Short bones like the carpal bones function as points of absorption of pressure and distribution of shearing forces. They are made of compact bone.

Joints

Joints may be classified as fibrous, cartilaginous or synovial (Fig. 18.1).

Type of joint	*Range at movement*	*Examples*
Fibrous joint	Nil	Cranial sutures, tibiofibular joint
Cartilaginous joint	Limited	Intervertebral joint, symphysis pubis
Synovial joint	Wide	Hip, knee, elbow

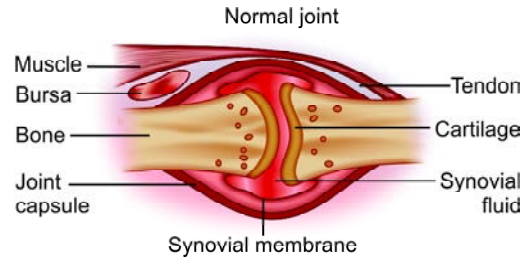


Fig. 18.1: Structure of a synovial joint

In a synovial joint, the bone ends are capped by hyaline cartilage. At the osseochondrous junction, synovium is attached to bone reflected from it to line the joint cavity. Outside the synovium is the tough fibrous capsule which is thickened in some areas to form ligaments. The capsule and ligaments prevent excess movement at the joint. In joints like the knee, there are fibrocartilaginous pads or menisci which serve to appose the articulating surfaces properly. The synovial fluid and synovium reduce friction during movement. Bursae prevent friction between tissues around a moving joint. These are similar to synovium in structure, function and disease susceptibility. Synovium is highly vascular. Structurally, the synovium presents an ideal stage for humoral and cellular immune reactions. Synovium has only very few nerve endings and cartilage has none. Articular cartilage is avascular. It derives its nutrition from materials passing into it from bone or synovial fluid. Articular branches of blood vessels enter at the joint margin.

The points of attachment of tendons and ligaments to bone are called entheses. The joint capsule, entheses, ligaments and tendons are rich in nerve endings that perceive pain and proprioception. When a joint is inflamed, reflexogenic nerve endings cause reflex contractions of neighboring muscles leading to painful stiffness.

The main function of all synovial joints is to allow stable, controlled movements. Muscles of the locomotor system are all striated muscles. They are all under voluntary control.

DISEASE PATTERN AFFECTING THE LOCOMOTOR SYSTEM IN INDIA

Numerically, traumatic fractures, dislocations and other lesions head the list. These fall into the realm of orthopedics.

Rheumatological disorders contribute to the rest of the diseases of the musculoskeletal system and connective tissues. *Osteoarthritis* accounts for 30% of the musculoskeletal morbidity Soft tissue rheumatism constitutes around 20% of musculoskeletal problems. *Low backache, sciatica osteoporosis,* and problems related to defective posture and lack of exercise are common in clinical practice.

In India, rheumatic fever merits a special mention since it is common in children and adolescents and it leads to lifelong crippling cardiac sequelae. In recent years, postviral arthritis secondary to chikungunya infection is a major cause of joint problems in south Indian states like Kerala, Karnataka, Andhra Pradesh and Tamil Nadu. Osseoarticular tuberculosis is also common in children and adults, the osseous focus being in the metaphysis in children and in the epiphysis in adults. Tuberculosis can also cause an allergic reactive arthritis resembling rheumatoid arthritis called ***Poncet's disease***. Many systemic diseases may present with arthritis; these include *hypothyroidism, diabetes mellitus, acromegaly, bleeding disorders, myeloproliferative disorders, AIDS,* drug reactions and other conditions.

The inflammatory group of arthritis constitute only around 10 to 12% of all musculoskeletal diseases in India.The major causes of inflammatory arthritis are the seronegative spondyloarthritis, and diffuse connective tissue diseases (DCTDs).

Seronegative spondyloarthropathies constitute seronegative spondyloarthropathies around 7% of musculoskeletal problems in India. The important subtypes of spondyloarthropathies are ankylosing spondylitis, Reiters syndrome or reactive arthritis, psoriatic arthritis, arthropathy of inflammatory bowel diseases and undifferentiated spondyloarthopathy.

The most important DCTD is rheumatoid arthritis with a prevalence of around 0.5 to 2% among the general population. The other major members of DCTDs are systemic lupus erythematosus, progressive systemic sclerosis, and inflammatory muscle diseases. Any of the DCTD may be associated with *Sjögren's syndrome* which is common. Each of the DCTDs can overlap with each other as in mixed connective tissue disease and progress on to other forms. Other causes of inflammatory arthritis are crystal induced synovitis like gout, and primary vasculitic syndromes.

The pattern of rheumatological disorders differ in different age groups. In children, the common problems seen are growing pains, hypermobility, hip pain due to several causes, traumatic lesions of knees, rheumatic fever, osteomyelitis, septic arthritis, juvenile rheumatoid arthritis (JRA), rickets

and others. In the young adult male, seronegative spondyloarthritides and postviral arthritides are common. During the sexually active periods of life, arthritic complication of sexually transmitted diseases are more common.

In pregnancy and the puerperium low back pain is nearly universal and sciatica is common enough. The postmenopausal age is associated with bone and joint symptoms. Osteoporosis proceeds rapidly after menopause. Hypothyroidism, depressive illness and osteoarthritis are common causes of rheumatic symptoms in this group. Degenerative joint diseases such as osteoarthritis of several joints, cervical spondylosis, sciatica and lumbar canal stenosis are more common in elderly. Those exposed to repeated occupational trauma during work develop osteoarthritic changes of particular joints early.

Occupation and environment can modify joint diseases, particularly osteoarthritis, e.g. *goalkeeper's fingers, bass player's thumb, Zulu dancer's hip,* and others. Tenosynovitis like the Achilles tendonitis of long distance runners and prepatellar bursitis in housemaid's knee are other examples of occupation-related rheumatism. Enthesopathies like lateral and medial epicondylitis of elbow (syn: tennis elbow and golfer's elbow) are common in Indian housewives who do clothes washing, grain grinding, pounding, etc. Factory workers inhaling metal or polymer fumes can get fever associated with arthralgias.

CHAPTER

19 Examination of the Musculoskeletal System

KV Krishna Das, Binoy Paul

History, Physical examination, General examination, General principles of examination of joints, Examination of particular regions

HISTORY

Taking a detailed and accurate history is very important to make a correct diagnosis in musculoskeletal diseases (MSKD) The cardinal symptoms of MSKD are pain, stiffness, swelling, limitation, of movement, weakness and fatigue.

Pain

The most important rheumatological symptom is pain. Find out the onset and duration of this symptom. Chronic joint pain occurs in osteoarthritis (OA), rheumatoid arthritis (RA), psoriatic arthritis, ankylosing spondylitis (AS), juvenile RA and others. Acute joint pain develops in rheumatic fever, traumatic arthritis, reactive arthritis, acute gout and in the acute phases of all chronic arthropathies. Osteomalacia and osteoporosis present with chronic aching pain over the spine and weightbearing bones, aggravated by activity.

Site of Pain

It is important to locate the site of pain clearly, whether it is from joints, bones, periarticular tissues, muscles, nerves or vascular lesions. Ask the patient to show the exact site of pain. Localization of pain to the enthesis should suggest periarticular lesions. Neuralgic pain over a dermatomal distribution occurs in involvement of the dorsal nerve roots. Symmetrical distribution of pain and numbness over the distal parts of the extremities is suggestive of nerve involvement, which may be mistaken for joint disease.

Joint Pain

Joint pain that is worst in the morning and gets relieved as the day advances, suggests inflammatory arthritis like rheumatoid arthritis. Pain that comes on by the end of the day and aggravated by joint use suggests osteoarthritis. Brief or fleeting joint pains that move quickly, i.e. flit from joint to joint must bring rheumatic fever to mind. Acute or subacute arthritis is the presenting feature in Juvenile rheumatoid arthritis (JRA). Several infections such as viral hepatitis B, infective endocarditis, leprosy (during reactions), brucellosis, syphilis, Lyme disease and others may present with arthritis as a major symptom. Acute leukemias in children commonly give rise to arthritic manifestations.

In children, pain of insidious onset with impairment of function of single joints may be the only feature of osteoarticular tuberculosis. Pain around the hip in a child may be due to tuberculosis or Perthe's disease. In the former, pain is more severe and unrelieved by rest and invariably, it disturbs sleep. The latter often presents with slight pain, a limp and restricted movement.

Septic arthritis presents as severely painful acute arthritis. Acute gouty arthritis presents as sudden onset of pain, swelling and signs of inflammation characteristically in the metatarsophalangeal joint of the big toe. Several other joints may also be affected. Chronic gout presents with pain, restriction of movements and deformities of several joints—big and small. Recurrent joint pains and swelling

involving whole foot, hands or digits in children should suggest dactylitis occurring in sickle cell disease which is widespread in India.

Vague discomfort followed by severe pain and swelling of the major joints like knees, elbows, hips or ankles may be the presenting symptom in hemophilia.

Absence of pain, in the presence of gross abnormalities should suggest neuropathic joints such as occurring in syringomyelia, tabes dorsalis and diabetic neuropathy.

Periarticular Pain

Typically, patients relate the pain to activity. Wringing clothes can bring on the acute pain of a tennis elbow. The pain of plantar fascitis is felt most when walking in the morning or getting up after sitting for a fairly long time. The first few steps are the most painful and on hobbling around for sometime the pain decreases. Pain around the shoulder with stiffness and limitation of movement is typical of periarthritis shoulder which is more common in diabetes. Low backache associated with tender nodules over the sacroiliac region is suggestive of soft tissue lesions like fibrositis.

Muscle Pain

Muscle pains are felt more over the big muscles, in the calves, over the upper part of the trunk posteriorly, around the shoulder, and low back. The pain is usually aching in nature and associated with tenderness. Pain worsens by putting the muscle into action. Unaccustomed overuse of the muscle is a common cause. This pain is self limiting. Electrolyte imbalance, particularly hyponatremia and hypocalcemia may lead to severe muscle cramps which come on intermittently. Ischemia to muscle gives rise to claudication on exertion. Muscle weakness associated with pain and tenderness should suggest polymyositis or dermatomyositis. Bilateral shoulder pain associated with a raised ESR, weight loss and depression is seen in polymyalgia rheumatica. Systemic illness such as hypothyroidism may present with muscle pain in the upper thoracic region, shoulders and trunk, especially in women. Wandering muscle pains and tenderness associated with irritability, insomnia, hyperesthesia and multiple vague complaints may be a manifestation of depressive illness. Several infections such as leptospirosis lead to severe myalgia.

Bone Pain

Pain arising from fractures or other traumatic lesions can easily be identified. In osteoporosis, fractures may result even from trivial trauma and may often be unnoticed. Secondary deposits from cancer and diseases like osteogenesis imperfecta give rise to painless pathological fractures. Children may complain of deep and severe pain in the thigh and legs coming on and off, worse at night, lasting for over three months at a time. These are termed "growing pains" of bones and these typically respond to local applications and reassurance. In multiparous women, a nonspecific ache around the shoulders, radiating to the back and thighs, associated with proximal muscle weakness may be the early presentation of osteomalacia. Lesions of the vertebral column such as tuberculosis, multiple myeloma and secondaries give rise to pain on assuming the erect posture and on movement. Jarring movements such as travel in an autorickshaw are particularly resented. In prolapse of the intervertebral disk, coughing and sneezing give rise to sharp pain with radiation along the nerve roots. These may manifest as girdle pain or sciatica. This is due to compression of the posterior nerve roots. In ankylosing spondylitis, pain starts over the lumbosacral region and spreads to other parts.

Neuralgic Pain

Pain of peripheral neuritis is burning in character or "pins and needles" sensation affecting the distal parts of the extremities more. Pain caused by compression of the dorsal nerve roots have lightning like quality and they have a dermatomal distribution. Entrapment neuropathies lead to pain in the distribution of the compressed nerve. Compression of the median nerve in the carpal tunnel causes symptoms distal to it, like numbness, pricking and burning sensation, worse at night and aggravated by activity. Compression of the lateral cutaneous nerve by deep fascia in the thigh leads to pain over the lateral aspect of the thigh—***meralgia paresthetica***. The pain of lumbar canal stenosis and neurogenic intermittent claudication comes on when the patient uses his lower limb. In neurogenic intermittent claudication the lower extremities become numb and weak as the patient walks. On resting, the symptoms disappear. This is due to ischemia of the lower segments of the spinal cord and spinal nerve roots (Figs 19.1 to 19.5).

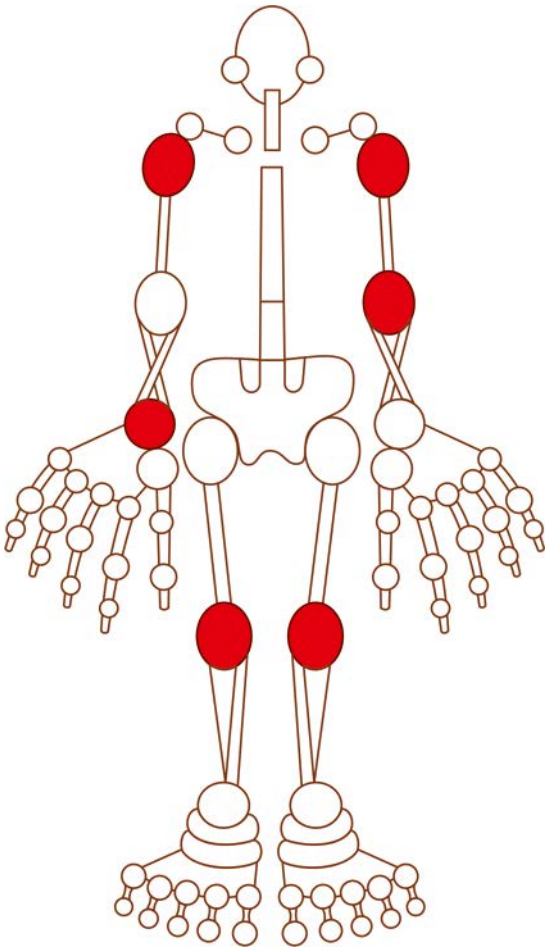


Fig. 19.1: Site of pain (marked red) in polyarthritis



Fig. 19.2: Sites of claudication



Fig. 19.3: Pain of sciatica



Fig. 19.4: Site of pain—sacroiliac joint involvement



Fig. 19.5: Distribution of pain in meralgia paresthetica

Vascular Pain

This takes the form of intermittent claudication in the early stages, when the main arteries are occluded. Cramp-like pain is felt during activity over the exercising muscles. It is relieved by resting, to reappear when activity is resumed. As the vascular occlusion extends to the smaller arteries, excruciating pain develops over the distal parts of the extremities, felt even while resting. The part is cold with absence of pulsation in arteries. Later bluish discoloration develops suggesting the onset of gangrene.

Other Painful Conditions

In many instances, the same lesion may cause pain by several mechanisms. For example, cervical spondylosis causes joint pains, periarticular pain, pain of reflex muscle spasm in the neck, pain of nerve root compression as well as vascular insufficiency. Painful limitation of movement of shoulders is common in diabetes and impaired glucose tolerance. Stiffness of the back may occur due to inflammatory diseases of the spine or secondary to irritation of nerve root by other causes. Irregular fever, weight loss with focal pain and spasm must alert one to the possibility of tuberculosis of the spine. Local tenderness and pain over the vertebrae developing in an elderly person should suggest malignant secondaries.

An acute backache with limitation of movement occurring in a postmenopausal woman or elderly

person is commonly due to compression fracture of osteoporotic vertebrae. A stiff hip in a child or young adult with flexor spasm could be due to conditions as diverse as appendicitis, cold abscess in the groin, Perthe's disease or tuberculosis hip. Stiffness of the knee with difficulty in squatting, occurring in later life is commonly due to osteoarthritis. In addition to rheumatological disorders, several neurological disorders such as parkinsonism, upper motor neuron lesions, mytonias and dystonias increase muscle tone and ache. These have to be identified by proper examination.

Deformities

Many patients complain of progressive or acute deformities of skeletal structures. These lesions may be painful or painless. The common painless deformities include rickety rosary, pigeon chest and bow legs in rickets. Gradual shortening of vertebral column and thoracic kyphosis in osteoporosis (*Dowager's hump*), progressive kyphosis with flexion of cervical spine in ankylosing spondylitis, Heberden's nodes over terminal phalanges in osteoarthritis, nodules of varying sizes in rheumatoid arthritis and tophaceous gout may be painless or can become painful. Increase in the size of the head is seen in Paget's disease. Neuropathic joint deformities seen in diabetes mellitus, tabes dorsalis and syringomyelia are all totally painless.

Progressive painful deformities of joints with loss of function occur in rheumatoid arthritis, gout, osteoarthritis and psoriatic arthritis (Figs 19.6 to 19.9). Extra-articular features are also common (Figs 19.10 to 19.21). Tuberculosis, myeloma, malignant secondaries, fluorosis and osteoarthritis, are common to produce vertebral deformities.



Fig. 19.6: Early RA with swelling of PIP joints (spindling of fingers)



Fig. 19.8: Boutonniere deformity in RA—flexion at PIP joint with extension at DIP joint



Fig. 19.7: Flexion at DIP joint with hyperextension at PIP joint in RA (Swan neck deformity)

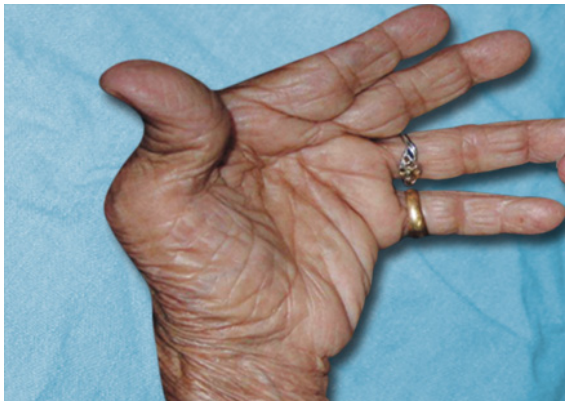


Fig. 19.9: Z-deformity of thumb with ulnar deviation in RA



Fig. 19.10: Multiple oral ulcers in Behcet's syndrome



Fig. 19.11: Large scrotal ulcer in Behcet's syndrome

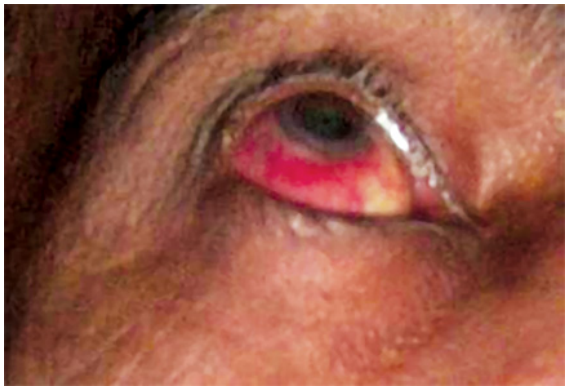


Fig. 19.12: Uveitis in ankylosing spondylitis

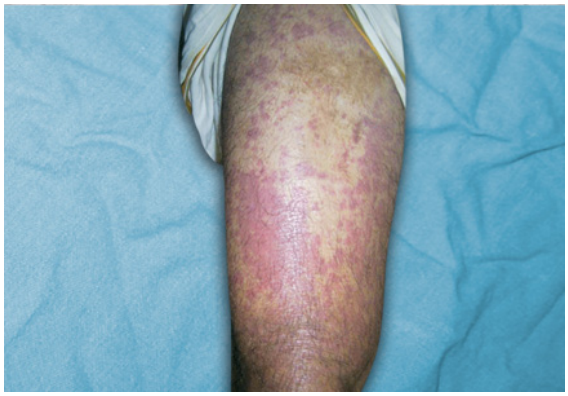


Fig. 19.13: Henoch Schonlein purpura



Fig. 19.14: Alopecia and skin rash in the forehead in SLE



Fig. 19.15: Butterfly rash in the malar area sparing nasolabial fold in SLE

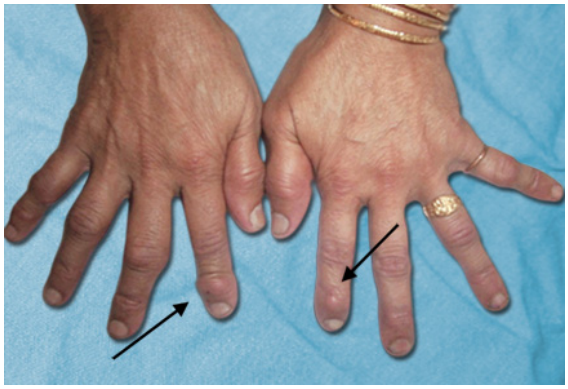


Fig. 19.16: Osteoarthritis hand. Arrows point to Heberden's nodes



Fig. 19.17: Symmetrical arthritis of PIP and MCP joints and wrist in RA



Fig. 19.20: Psoriatic arthritis—DIP joint involvement with pitting of nails



Fig. 19.18: Ruptured extensor tendons with "drop" of fingers



Fig. 19.21: First metatarsophalangeal joint involvement with a tophus (arrow) in gout



Fig. 19.19: Hematoma thigh with hemarthrosis left knee in hemophilia

Pattern of Joint Involvement

The number of joints involved and their distribution helps to diagnose the cause of arthritis. Single joint disease is called *monoarthritis*, involvement of four joints or less is called *pauciarticular arthritis*, involvement of 5 or more joints is called *polyarthritis*. Polyarthritis may be symmetrical as in rheumatoid arthritis or asymmetrical as in seronegative spondyloarthritis. Arthritis may be acute or chronic.

At any point of time, factors such as unaccustomed exertion, intercurrent infection, dietary or alcoholic excess, minor trauma, vaccination, surgery, drugs, mental stress and physical stress can exacerbate these arthritides and therefore these factors should be elicited in history.

Clinical Points to Distinguish the Common Chronic Polyarthritides

Rheumatoid Arthritis

Bilaterally symmetrical joint lesions, especially of the small joints of the hands and feet with affection of larger joints and characteristic morning stiffness lasting for more than one hour after waking, is suggestive. Complete resolution is unlikely. Progressive deformity results and disease extends over several decades.

Palindromic rheumatism is the occurrence of recurrent episodes of acute monoarthritis, often resembling gout, yet lasting only for 24 to 48 hours. Many of them who are positive for rheumatoid factor and *Anti CCP* develop chronic rheumatoid arthritis on follow-up.

Osteoarthritis: Insidious onset, affects spine and weightbearing joints like knees and hips and small joints of fingers asymmetrically, e.g. first carpometacarpal joint, first metatarsophalangeal joint and distal interphalangeal joints.

Seronegative spondyloarthritis: Affects sacroiliac region and low back with asymmetric peripheral joint involvement of lower limbs.

Psoriatic arthropathy: Asymmetric involvement of distal interphalangeal and metacarpophalangeal joints, other joints are affected at random.

Gout: Peripheral joints of hands and feet are affected in early stages. Pain in acute gout typically starts at night and peaks in a few hours. The first metatarsophalangeal joint is affected most frequently. The term *"podagra"* refers to the severe pain in the instep. Chronic tophaceous gout involves larger joints—tophi are common.

Pseudogout (acute synovitis due to calcium pyrophosphate deposition): Knees, wrists, elbows, shoulders and hands are involved, more common in elderly women.

Rheumatic arthritis: Acute arthritis of large joints with effusion. The joints are affected one after another with clearance of the affected joints and affection of newer ones. Complete resolution of arthritis is the rule. Occasionally a chronic deforming arthropathy may develop especially in the hands (Jaccoud's arthritis).

Systemic lupus erythematosus: Butterfly shaped rash in the malar area with arthritis is classical (Fig.19.15). Systemic involvement like fever, renal disease, pleurisy or effusions are common. Joint deformities are caused commonly by subluxation and not destruction of tissue and they are reversible.

Acute Arthritis

Common causes include trauma, pyogenic arthritis, rheumatic fever, rheumatoid arthritis, gout, Henoch-Schonlein syndrome, reactive arthritis in Reiter's syndrome, gonococcal arthritis, syphilitic arthritis, hemophilia, serumsickness, allergic disorders.

Monoarthritis

Two thirds of all gout, pseudogout and calcific periarthritis occur initially in the first metatarsophalangeal joint, knee or shoulder joint. Hemarthroses tend to occur in large joints-knee, elbow, wrist or ankle. Single hip joint involvement in children is often due to tuberculosis or Perthe's disease; septic arthritis can involve any joint. Besides these, rheumatoid arthritis, Reiter's syndrome, osteoarthritis, ankylosing spondylitis, juvenile rheumatoid arthritis and pyrophosphate arthropathy can present as monoarthritis.

Systemic Involvement in Rheumatological Disorders

Rheumatological disorders often involve other systems (Table 19.1). Enquire about skin rashes, hair loss, subcutaneous nodules and oral and genital ulcers. Eye symptoms such as photophobia, pain and redness may be present. Gut symptoms commonly encountered are dysphagia occurring in progressive systemic sclerosis, dyspepsia caused by reflux esophagitis or drug induced gastritis, and melena usually secondary to drug induced gastroduodenitis. Respiratory, cardiovascular and nervous systems may be affected in many instances. Several systemic diseases may present with rheumatological symptoms and signs.

PHYSICAL EXAMINATION

General Examination

Rheumatological examination begins the moment the patient enters the doctor's room. Watch his gait. A slow painful gait and deformities may be apparent at first sight itself. Always ask the patient to strip before examination. Patients with frozen shoulders have difficulty in removing their clothes and those with hand problems find it difficult to manipulate the buttons (Figs 19.22 and 19.23).

General examination has to be done as in any other medical case. However, as one scans the patient from head to toe, the following points require emphasis:

Hair loss in SLE, skin and nail changes of psoriasis, prominence of the superficial temporal arteries and scalp tenderness in giant cell arteritis and eye lesions such as conjunctivitis in Reiters syndrome, episcleritis and scleritis in rheumatoid disease.

Table 19.1: Common systemic diseases which may present with rheumatological symptoms

Diabetes mellitus	Stiff hands, frozen shoulders, Dupuytren's contracture, osteoarthritis, gout, chondrocalcinosis, septic arthritis, forefoot osteolysis and neuropathic joints
Hypothyroidism	Non-articular rheumatism, arthritis, proximal myopathy
Hyperparathyroidism	Rarefaction of bone, vertebral collapse, chondrocalcinosis, metastatic calcification
Acromegaly	Backache, hypermobility, carpal tunnel syndrome, arthritis, Raynaud's phenomenon
Leukemias	Mono /pauci / polyarthritis, vertebral collapse, bony swellings, secondary gout
Carcinoma lung	Hypertrophic osteoarthropathy at wrists and ankles
Cancer of prostate/ Bronchus	Seronegative RA-like arthritis which may antedate tumor
Pancreatic cancer	Subcutaneous nodules, eosinophilia, seronegative RA-like picture which may antedate tumor, deep venous thrombosis
Occult malignancy of ovary, uterus, lung, breast and stomach	Dermatomyositis, polymyositis
Lymphoma, polycythemia rubra vera Chronic renal failure Corticosteroid therapy	 Secondary gout Renal osteodystrophy Osteoporosis
Inflammatory bowel diseases	Reiter's syndrome
Allergy-serum sickness, drug allergy Infections: tuberculosis, brucellosis, Lyme arthritis syphilis, leprosy in reaction Dermatological disorders - psoriasis Nutritional disorders —rickets, osteomalacia, osteoporosis Congenital diseases— Paget's disease of bone achondroplasia, chondrodysplasia, Marfan's syndrome and others	Polyarthralgia, arthritis Various forms of spondylitis pauci or polyarthritis Polyarthritis Bone deformities, bone pains fractures Various rheumatological Symptoms, deformities fractures

Some characteristic diagnostic features which have to be spotted at the first sight itself include the butterfly rash over the face in SLE, small oral aperture (fish mouth) with tight thickened skin of the face in scleroderma, dryness of mouth and eyes in Sjogren's syndrome and the reddish periorbital edema of dermatomyositis.

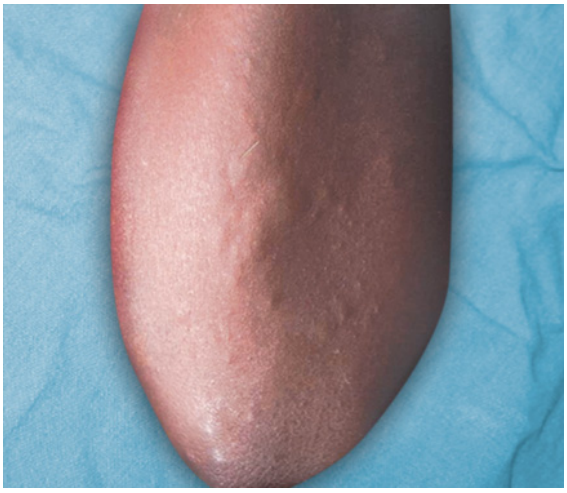


Fig. 19.22: Rheumatic nodules appear in crops around the elbow

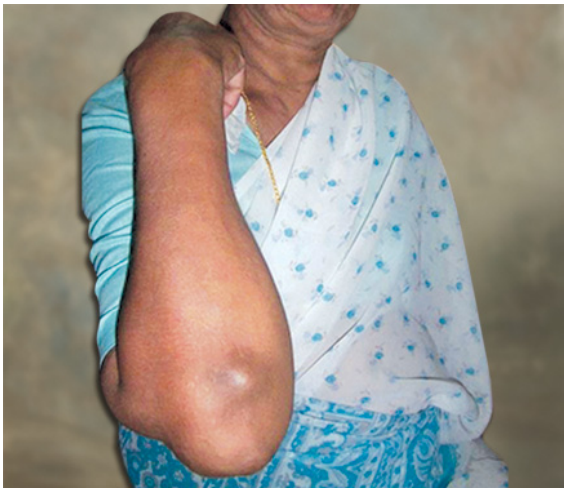


Fig. 19.23: Rheumatoid nodule around the elbow joint

In India, lepromatous and neural leprosy may masquerade as joint problems, especially during reactions. It is important to bear this in mind.

Subcutaneous nodules should be looked for though the patients may not be aware of their presence. Commonly they are seen around bony prominences. Non-tender nodules occur in RA, chronic gout, and rheumatic fever. Tender nodules such as erythema nodosum may be due to drug reaction, streptococcal infections, SLE, leprosy, tuberculosis, lymphoreticular malignancies or Behcet's syndrome (Fig. 19.10). Look at the fingers for signs of digital vasculitis and nail fold infarcts.

GENERAL PRINCIPLES OF EXAMINATION OF JOINTS

Points to be noted:

1. Whether joints are affected or not, if so mono- or polyarticular.
2. Identification of anatomical abnormalities.
3. Determination of the loss of function, and
4. Identification of the causes of lesions.

The scheme for general examination of all joints is the same. In addition, special maneuvers are available for bringing out abnormalities in particular joints. Physical examination consists of inspection, palpation and assessment of the range of movement.

Inspection

Note the following:

1. Posture of the affected part in the resting position.
2. Color.
3. Swelling and deformities.
4. Wasting of muscles.

Posture of the affected part: When a joint becomes painful, muscle spasm develops and the part is held in a position of maximum relief from pain and all movements are avoided. In general, the position adopted is the one in which joint space is maximal, e.g. 10° flexion of the knees, flexion of the elbow, neutral position of the wrists. Any attempt to move the part or even tap on the bed is strongly resented.

Color: Look for redness or other changes in color. In acute arthritis, the skin is red and often edematous. Bruising may be seen over hemar-throsis (bleeding into joints) and in traumatic arthritis.

Swelling and deformities: Most of the superficial joints have hollows around them, e.g. anterior and posterior aspects of the outstretched elbow, hollows on either side of the patella in the extended knee, and anatomical snuffbox in the wrist. These hollows are filled either due to effusion or edema of articular and periarticular structures early during joint diseases. When the lesion becomes more advanced, the joint is swollen as a whole.

Wasting of muscles: Long-term disuse of the joint results in wasting of the muscles which move the joint. Wasting is partly due to involvement of the muscle also by the same disease process, e.g. rheumatoid disease. Wasting is assessed by comparison of the bulk of the muscle on either side of the joint and comparison of the circumference of the limb over the corresponding points both proximally and distally.

Procedure of Measurement of Limb Circumference

Mark out corresponding points over both limbs by measuring the same distance away from a fixed bony point, e.g. tip of the medial malleolus of the tibia, tubercle of the tibia, or greater trochanter of the femur. Measure the girth of the limbs over these points. Normally the measurements do not differ more than 1.5 cm, the right sided limbs being larger in right handed individuals, and vice versa. Any differences greater than this should suggest wasting, provided the other limb is normal.

Palpation

Joint structures are extremely painful and tender when inflamed. Therefore great care should be taken to avoid hurting the patient.

Temperature: Skin over normal joint is slightly colder than the rest of the body. Elevation of temperature occurs in inflammatory joint disease.

Tenderness

Elicit tenderness by gentle pressure. Identify the site of maximum tenderness with a view to decide whether the joint space, bony points, capsule, ligaments, entheses, tendons or bursae are the sites of maximal affection. Severe tenderness suggests acute lesions such as septic arthritis, gout, rheumatic fever or hemarthrosis. In chronic arthritis, tenderness may be less marked. Tenderness can be graded by quantitating the pressure required to cause pain.

Absence of tenderness suggests degenerative arthritis. Neuropathic joints are painless and are not tender even in the presence of obvious deformity. Even gross manipulations do not elicit pain from them.

Identification of Anatomical Landmarks Around the Joint

Look for the anatomical bony landmarks with a view to identify displacements, if any. In fractures and dislocations the anatomical landmarks are altered. Determine whether the deformities are correctable by manipulation. Deformities caused by muscle spasm or inflammatory lesions can be identified from those caused by ankylosis, fractures and dislocations.

Palpate the hollows to determine whether they are filled and if so, for fluctuation. Fluctuation is obtained when the joint or bursa are filled with fluid.

Synovial membrane: Thickening of the synovial membrane can be identified in many of the superficial joints as boggy swellings along the line of synovial reflection. Synovial thickening is more marked in proliferative lesions like RA.

Fluctuation: Palpate with the index fingers of both hands and elicit fluctuation. Fluctuation in all directions suggests the presence of fluid underneath. Cross fluctuation can also be elicited between joints and bursae communicating with them, e.g. knee joint and suprapatellar bursa.

Periarticular structures: Palpate carefully the joint capsule for thickening and irregularity. Ligaments, tendons, bursae, and muscles should be examined for abnormalities. Severe tenderness over the ligaments, tendons and entheses should suggest involvement of these structures.

Look for pitting edema around the joint. Presence of edema suggests underlying inflammation.

Movements

Active movements: Active movements are those performed by the patient himself. Passive movements are those which are done by manipulation by the examiner. Always try active movements first, since passive movements may cause severe pain if the joint lesion is acute.

For testing active movements, the patient is asked to move the joints over the full range in all directions relevant to the joint. Degree of limitation is noted. See whether the limitation is due to restriction of joint mobility, pain, or weakness of muscles. Palpate the joint during movement to elicit crepitus.

Passive movements: After testing active movements, perform passive movements by moving the joints in all directions without active participation by the patient. Passive movements help to assess the range of movements, elicit tenderness and crepitus and also identify structural abnormalities that restrict movement. Apart from painful joint lesions, movement is restricted by fusion of the joint space (ankylosis), which may be fibrous or bony. A small range of movement is possible in fibrous ankylosis whereas none is possible in bony ankylosis. Exostoses are bony growths which may restrict joint movements if they arise near joints. Ruptured menisci and cartilages, and loose bodies within joints (joint mice) can be identified. Range of movements in any joint can be measured by a goniometer. Appendix-1 gives the normal range of movements of various joints.

Muscle power is tested by asking the patient to contract his muscles against resistance. Conventionally, for neurological examination muscle power is graded as given below:

Grade 0: No movement
Grade 1: Only a flicker of movement
Grade 2: Movement is possible if gravity is eliminated
Grade 3: Movement against gravity is possible
Grade 4: Movement against partial resistance is possible.
Grade 5: Normal power.

Apart from muscle weakness due to neurological causes, painful joint lesions lead to loss of power. For example, the hand grip is weakened in arthritis involving small joints of the hand. As the joint lesions subside, the grip becomes stronger. Improvement in power is a good parameter to assess progress of joint disease. The power of muscle groups can be quantitated by using a dynamometer.

Examination of Joints Above and Below

It is common for joint pain to radiate proximally or distally depending on the innervation. Pain arising from the cervical vertebrae may be felt as shoulder pain radiating further down. In hip lesions pain may be referred to the knee and these may masquerade as diseases of the knee, e.g. tuberculosis of hip. In carpal tunnel syndrome, pain may radiate proximally to the elbow and shoulder. It is therefore important to examine the proximal and distal joints before completing the examination.

When confronted with a joint problem, examine the maximally affected joint first and then proceed to make a total skeletal survey. It is advisable to have a routine scheme so that no joint will be missed. Starting from the jaw proceed downwards to cervical spine, shoulder girdle, upper limb, thoracic spine, lumbar spine, pelvis and lower limbs.

Posture and Gait

Posture

Normal spine in the adult has lumbar lordosis, and kyphosis in the thoracic and cervical regions. This alignment of the spine may be altered by muscle spasm and lesions of the vertebrae, intervertebral discs or ligaments. Shortening of the vertebral column and upper thoracic kyphosis occur in post-menopausal osteoporosis. Osteoarthritis leads to osteophyte formation, nerve root compression and deformities more commonly in the cervical and lumbar regions. Progressive kyphosis involving the whole of the vertebral column develops in ankylosing spondylitis. Skeletal fluorosis leads to limitation of movements which can be severe in the later stages. Exaggeration of lumbar lordosis occurs in myopathies affecting spinal muscles. When the vertebral lesion affects several vertebrae the deformity is smooth. When one or two vertebrae alone are affected an angular deformity develops (gibbosity).

Gait

Rheumatic disorders alter the normal gait due to pain, progressive deformities of joints and limitation of movement. This leads to obvious limping and shortening of the steps. The patient avoids weightbearing on the painful extremity.

EXAMINATION OF PARTICULAR REGIONS

Head and Neck

The head, neck and upper trunk are examined with the patient seated on a stool.

Temporomandibular joint: Ask the patient to open and close the mouth and to move the lower jaw sideways and back and forth. Note pain, tenderness and crepitus, indicative of temporomandibular arthritis.

Ossicles of the ear: Test auditory function-Conduction deafness may occur in rheumatoid disease due to affection of the synovial joints between ear ossicles.

Joints of the larynx: Cricoarytenoid joint involvement in rheumatoid arthritis may give rise to hoarseness of voice and stridor.

Sternoclavicular and sternocostal joints: Inspect the front of neck and chest. Note if the sternoclavicular and sternocostal joints are swollen and tender.

Cervical spine: Inspect the back of the head, neck and chest. Remember that the cervical spine extends above the hairline. Look for muscle wasting. In severe ankylosing spondylitis, cervical kyphosis may be so severe that the patient cannot look to the front. Palpate back of head, cervical spine and thoracic spine for deformities and tenderness. Tenderness in the suboccipital region and shoulder girdle is an important sign of lesions of the cervical spine.

Check movements of the neck, i.e. flexion, extension, lateral flexion and rotation.

Movements of the neck may be restricted by lesions of the spine or painful lesions of the muscles or other soft tissues. Disc lesions and spondyloses may restrict movement in all directions but usually rotation and lateral flexion to one side are affected more. In atlantoaxial disease the patient may complain of vertigo or diplopia on rotation of the neck due to pressure on the vertebral arteries. Vascular complications of cervical spondylosis lead to vertebrobasilar insufficiency in certain positions of the neck. In rheumatoid arthritis, atlantoaxial subluxation may develop giving rise to a clunking sound on neck flexion. Rupture of the transverse ligament of the atlas gives rise to sudden compression of spinal cord.

Shoulder

Examination of the shoulder includes the study of the glenohumeral joint, acromioclavicular joint, rotator cuff, bursae and bicipital tendon. During inspection look for wasting of muscles. Fullness on the anterior aspect may be a sign of effusion. Palpate the joint margin anteriorly below coracoid process to detect joint line tenderness. While checking movements it is important to fix the scapula by holding it with one hand and eliciting glenohumeral movement with the other. Restriction of abduction and lateral rotation point to shoulder joint disease.

Local tenderness over the acromioclavicular joints and pain on shrugging shoulders are suggestive of acromioclavicular joint involvement.

Pain localized to the deltoid region suggests rotator cuff lesions. Ask the patient to abduct the shoulder while applying resistance. Limitation and

pain indicate *supraspinatus tendonitis*. Inability to initiate abduction occurs in total rupture of supraspinatus tendon. Weakness of abduction may be due to *partial tendon rupture.* Pain on forced external rotation indicates *infraspinatus tendonitis.*

Subacromial bursitis can mimic supraspinatus tendonitis, but here there is no pain on abduction against resistance.

Pain radiating down the front of the arm with tenderness along the bicipital groove occurs in *bicipital tendonitis.* Supination of flexed elbow performed against resistance worsens the pain.

Elbow

During inspection note if there is swelling or a flexion deformity. Swelling is usually apparent first in the paraolecranon grooves. A localized swelling over the olecranon may be due to olecranon bursitis. Palpate both epicondyles. Tenderness of the lateral epicondyle and pain aggravated by dorsiflexing wrist against resistance occurs in lateral epicondylitis *"tennis elbow"*. Tenderness of the medial epicondyle and pain aggravated by active flexion of wrist and resisted pronation points to medial epicondylitis—*Golfer's elbow* (Figs 19.24 to 19.27).

Radioulnar joints: Pronation and supination are movements taking place at these joints. In disease affecting these joints pronation and supination are restricted and painful. Local tenderness may be elicited over these joints.

Hand and Wrist

Inspect both hands with fingers in extension. Look at the dorsal and volar aspects. Note if there is obliteration of normal hollows due to inflammation.



Fig. 19.25: Tennis elbow—aggravation of pain on dorsiflexion against resistance

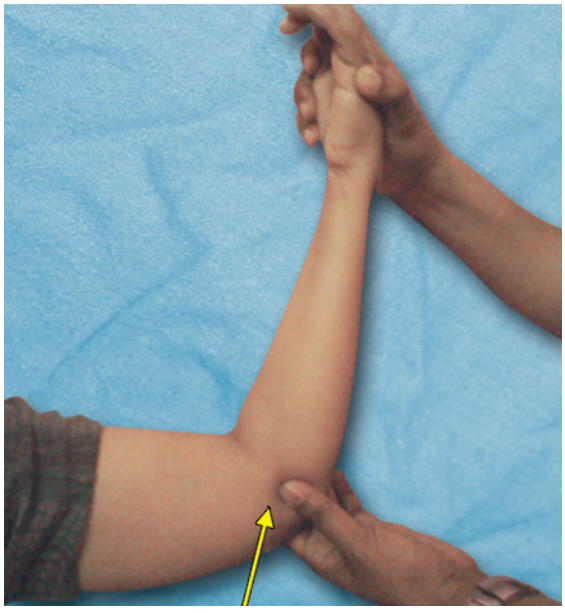


Fig. 19.26: Golfer's elbow—site of tenderness (arrow)

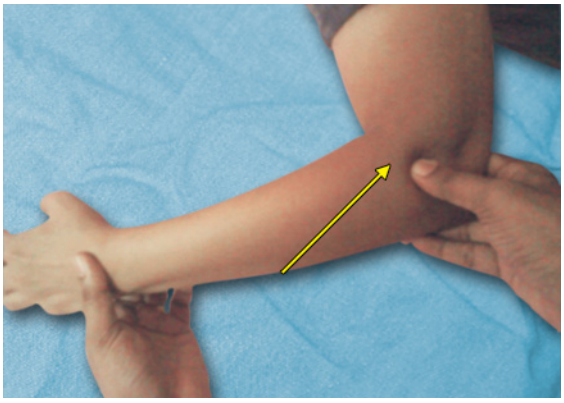


Fig. 19.24: Tennis elbow—site of tenderness (arrow)



Fig. 19.27: Palpation of wrist joint

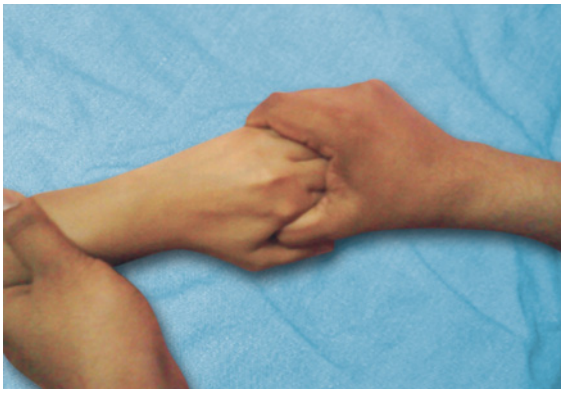


Fig. 19.28: Metacarpal squeeze



Fig. 19.29: Palpation of MCP joints

The groove between metacarpal heads may be obliterated due to synovitis. Look for muscle wasting. Ganglia are seen as small swellings on the dorsum near the wrist. Note if there are deformities.

Palpation and movement are best conducted from proximal to distal parts. Hold the wrist in a pinch grip with the examiner's thumb on the dorsum and fingers on the volar surface. Tenderness elicited by pressure indicates synovitis (Fig. 19.29).

Flex and extend the wrist. Pain and limitation of movement indicate lesions in the radiocarpal joint, midcarpal joints, or 2nd to 5th carpometa carpal joints.

First Carpometacarpal Joint

Hold the base of the thumb in a pinch grip and apply pressure. Tenderness occurs in arthritis affecting the first carpometacarpal joint.

Metacarpophalangeal Joints

Squeeze the hand across all metacarpophalangeal joints. Such a grip worsens pain in metacarpophalangeal joint disease. Palpate individual joints 1 cm distal to flexed knuckles to elicit tendereness (Figs 19.28 and 19.29).

Interphalangeal Joints

Interphalangeal joint lesions are painful on pinch grip and passive movements. Tenderness is maximal at the dorsomedial and dorsolateral aspects of the joints, i.e. on either side of the dorsal extensor tendon expansion (Fig. 19.30).



Fig. 19.30: Examination of proximal interphalangeal joint

Flexor and Extensor Tendon Sheaths

To check the health of flexor tendon sheaths, ask the patient to make a tight fist. See whether fingers can be extended and flexed without problem. Note if there is "triggering", i.e. extension is jerky and arrested midway. Palpate for nodules in the tendon sheaths. Nodules may be palpated when there is trigger finger.

How does one determine whether limitation of movement and pain are due* to *joint disease or tendon disease? A simple rule of thumb is to check the range of movements with the tendon concerned at a maximally relaxed position. For example, if a proximal interphalangeal (PIP) joint has a flexion deformity, in order to know whether the flexion is due to diseased PIP joint or inflammation of flexors of PIP joint, the following test is done. Put the flexor of the PIP joint in the maximally relaxed position by flexing the MCP joint fully. Then ask the patient to extend the PIP joint. If some extension at the PIP

joint is possible, it suggests that the earlier flexion at the PIP joint was due to tendon involvement and not joint disease. On the other hand, if flexion of PIP joint is due to joint disease, no further extension of the joint will be possible even after relaxing the flexor tendon.

To assess the health of extensor tendons and their sheaths check whether finger extension is full and pain-free and if any swellings are present on the dorsum. Inability to extend a finger points to tendon rupture (Fig. 19.18). Partial loss of extension may be due to a slipped tendon .

Common Tendon Sheath of the Thumb

Examine for pain and tenderness over the radial styloid and enquire about its radiation into the hand or forearm, aggravated by movements of the wrist and thumb. This occurs in inflammation of the common tendon sheath of the abductor pollicis longus and extensor pollicis brevis ***(de Quervain's tenosynovitis)***. These patients have pain on ulnar deviation of the wrist with the thumb tucked inside flexed fingers ***(Finkelstein's sign)***. One may also elicit crepitus along the course of the tendons at the wrist.

Entrapment Neuropathies

These are caused by mechanical pressure and compression over nerve trunks or their branches by fascia, ligaments or bones. Entrapment neuropathy causing pain and numbness in the hand with or without muscle wasting must be looked for. In ***Carpal tunnel syndrome*** (Figs 19.31A and B), percussion over the flexor retinaculum may lead to shooting pain along the distribution of the median nerve in the hand (***Tinel's sign***). The same effect can be reproduced by keeping the hand in full flexion for a minute (***Phalen's sign***). Check the arm muscle bulk also. These muscles may be wasted in carpal tunnel syndrome.

Ulnar nerve compression causes pain in the little finger and medial half of the ring finger and medial margin of the palm. When the site of compression is near the elbow both dorsal and volar aspects of the hand are affected and percussion at the elbow reproduces the symptoms (Tinel's sign). When the nerve is caught distally in the wrist, symptoms are limited to the volar aspect of the palm.

Another example of entrapment neuropathy is ***meralgia paresthetica*** manifesting as pain over the lateral aspect of the thigh caused by compression of the lateral cutaneous nerve of the thigh between the anterior superior iliac spine and the inguinal ligament.

Other sites of entrapment neuropathies include pressure points over radial, suprascapular, femoral, obturator, posterior tibial, plantar and intercostal nerves.

Vascular pain: Vascular pain must not be forgotten. Vascular pain occurs in occlusive arterial disease, thoracic outlet syndrome and systemic diseases like



Fig. 19.31A: Carpal tunnel syndrome—sensory loss over the palmar aspect



Fig. 19.31B: Carpal tunnel syndrome—sensory loss over dorsum of hand

scleroderma and myxoedema. Dip the hand in ice-cold water to detect ***Raynaud's* phenomenon**. This is the occurrence of severe tingling, numbness and burning pain in the hands and forearm when exposed to cold.

Compression of the subclavian artery by a cervical rib may lead to dusky cyanosis of the hand and gangrene of finger tips. The radial pulse may be detected to be weaker on the affected side, especially when the hands are raised above the head.

Causalgia: Causalgia is the severe burning pain occurring spontaneously over the limb following injuries to the nerve. The other associated features are shiny atrophic skin and abnormalities of sweating.

Examination of the vertebral column
Normally aligned vertebral column (spine) has the cervical and lumbar lordosis and thoracic and sacrococcygeal kyphosis. This smooth contour is altered in diseases affecting the vertebrae, intervertebral discs or the paraspinal muscles. The movements of the spine are flexion, extension, rotation and lateral flexion.

The vertebral column should be examined with the patient sitting in bed and also standing up, whenever possible. Gibbous (Gibbus) is an angular deformity of the spine, visible and palpable. It is often the result of fractures, dislocation or diseases such as spinal tuberculosis. **Kyphosis** is exaggeration of the normal posterior curvature of the spine. Generalized kyphosis occurs in congenital lesions, osteoporosis, osteoarthritis, myeloma and others. Lateral curvature of the spine is termed scoliosis. This may be congenital due to defective development of the vertebral column or acquired as in paralytic poliomyelitis.

Cervical spine: This part of the vertebral column has the maximal range of multiple movements and it is a common site for degenerative changes (*cervical spondylosis*). Look for flexion, extension, rotation and lateral flexion of the cervical spine. Note the range of movement and presence of pain and tenderness. Congenital abnormalities in the cervical spine are not uncommon. These include atlantoaxial dislocation, fusion of vertebrae hemivertebrae and others. The craniovertebral junction may be the seat of several abnormalities such as platybasia, basilar impression, occipitalisation of the atlas and others. Shortness of the neck (total body height divided by neck length more than 13.86), low hair line (posterior hair line coming below C4 spine), and facial asymmetry are commonly associated with such congenital lesions.

Cervical spondylosis is a common cause for pain in the neck and referred pain to the shoulders and hands in middle aged and elderly persons.

Thoracic and Lumbosacral Spine

Look for gibbous, kyphoscoliosis of thoracic spine, crowding of ribs and muscle wasting. Note paraspinal muscle spasm if any. Tenderness and pain over insertions of intercostal muscles occurs in ankylosing spondylitis (AS). Tenderness of upper part of the back, shoulder and anterior chest muscles may be due to nonarticular rheumatism, masked depression, or hypothyroid state. With the patient seated, check movements of the thoracic spine and rib cage-flexion, extension, lateral flexion and rotation. Severe limitation of rotation occurs in ankylosing spondylitis (AS) due to apophyseal joint involvement. Pain on deep breathing may occur in tendonitis of intercostal muscles in AS and this may mimic pleuritic pain. The manubriosternal and costovertebral articulations are also affected in AS. Measure chest expansion is grossly reduced in AS.

Lumbosacral spine is better examined with the patient standing up. Note the contour of the spine. Lumbar lordosis is lost in AS. Check forward flexion, side flexion and extension. Flexion is markedly limited in disc prolapse. Both flexion and extension are limited in AS. In active AS, the progression of disability can be assessed by the **Schober's test**.

Schober's test: Mark the midpoint of a line connecting the two posterior superior iliac spines, indicated by the dimple of Venus. Draw another horizontal line 10 cm above the previous line which crosses the spine. Make the patient bend forwards fully and measure distance between the line again. The skin gets stretched and normally the lower point remains fixed and the skin between the lines stretches by 5 cm or more (Fig. 19.32). With progressive limitation of flexion of lumbar spine, the lengthening is restricted to less than 5 cm.

In apophyseal joint disease, extension is restricted. Put the patient in the prone position

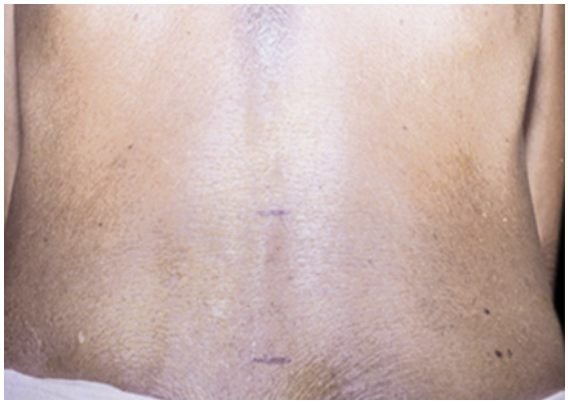


Fig. 19.32: Schober's test in ankylosing spondylitis (See the lines drawn at 10 cm apart)



Fig. 19.33: Straight leg raising test. This stretches the sciatic nerve

and palpate lumbosacral spines and sacroiliac joints for tenderness. Apply pressure over the coccyx to elicit tenderness. Pain over the coccyx is called ***coccydynia***. Assess muscle tone and note if trigger spots or painful nodules of fibrositis are present.

Straight Leg Raising Test

Straight leg raising test which elicits pain on stretching the sciatic nerve. With the patient lying supine and lower limb kept straight and foot slightly dorsiflexed, lift the leg. Pain over the hamstring muscles and limitation of movement indicate a positive test. Compare both sides. Normally the lower limb can be raised without discomfort to 100° from the horizontal. Limitation is commonly seen in irritation of the lower lumbar nerve roots, as occurring in disk prolapse or other compressive lesions (Fig. 19.33).



Fig. 19.34: Femoral strech. Flexing the knee and extending the hip to stretch the femoral nerve

Femoral Nerve Stretch Test

Flex the knee slowly while patient in prone position which produce pain in the anterior thigh due to stretching of the femoral nerve root. If this fails to produce pain gently extend the hip with knee still flexed (Fig. 19.34).

Hip

Examination of the hip region should bring out the following points.

1. Deformities
2. Abnormalities of joint function
3. Assessment of the state of health of tendons and bursae
4. Presence of hernias and other soft tissue lesions
5. Detection of lesions of nerve roots or nerve trunks which cause pain around the hip, and
6. Vascular abnormalities.

Gait: Make the patient walk. Note whether he leans on a stick held in the opposite hand and the pelvis lurches down on the side of weight-bearing. This is called ***antalgic gait*** and it is typical of painful lesions of the hip. External rotation deformities are also well brought out on walking, where the patient walks with the foot externally rotated.

Inspection: Inspect the hip region with the patient lying supine. Note the attitude of the limb. When there is a flexion deformity, the lumbar lordosis is exaggerated. When there is adduction deformity, the ipsilateral anterior superior iliac spine is elevated and there is an apparent shortening of the thigh. See which way the patellar surface points. This helps to

detect rotational deformities. Note if there is muscle wasting particularly of the quadriceps and glutei.

Palpate all the bony landmarks around. Note if there is pain mimicking sciatica associated with swelling and tenderness over the ischiogluteal bursa, which should suggest ***ischiogluteal bursitis***. It is best detected with the hip flexed.

Pain vaguely felt over the lateral aspect of the hip with tenderness anteriorly below the mid-point of the inguinal ligament should suggest hip joint disease.

Pain located anteriorly and tenderness along lateral border of femoral triangle made worse on forced flexion and extension of the hip occurs in iliopectineal bursitis.

Movements are tested with the patient lying flat. Flex the knees and hips to 90° and assess the degree of movement and pain produced by rotation. Internal rotation is often affected first. In patients with external rotation deformity internal rotation is virtually impossible. Always compare both sides. If dislocation is suspected flex the hip and knee to 90°, fix the pelvis with one hand touching the greater trochanter. With the other hand grasp the knee and push the thigh downwards towards the bed. Normally the femur and pelvis move as one unit and hence the trochanter is not felt to move relative to the pelvis by the hand which fixes the pelvis as well as touches the trochanter. If however, there is a dislocation of the hip, a non-union of an intracapsular fracture or total destruction of femoral head, then the trochanter moves with the thigh relative to the pelvis, i.e. it "telescopes".

Patrick's sign is a simple test to screen for hip disease. The patient lies supine. The examiner flexes, abducts and externally rotates the leg being tested such that the foot of the tested leg is on the top of the opposite knee. Next the leg being tested is slowly lowered towards the examining table. If the test leg falls at least parallel to the opposite leg the test is negative—no disease. If the leg remains abducted the test is positive indicating hip disease, ileopsoas spasm or sacroiliac disease.

The ***Ortolani's sign*** detects congenital hip dislocation in infants. The supine infant's hip are flexed and the examiner grasps the legs of the infant so that the examiner's thumbs are against the inner thighs and the fingers cover the lateral side of the thighs. Gently the hips are abducted and laterally rotated. Normally only after 30° to 40° of lateral rotation and 70° abduction is resistance felt. If before abduction of 70° a click is felt, Ortolanis sign is positive. This test should not be done repeatedly as it can damage the articular cartilage on the femoral head.

Galeazzi's sign helps detect unilateral congenital dislocation of the hip in children below 18 months of age. The child lies supine with hips and knees flexed at 90°. Normally both knees are at the same level; if one is higher than the other the test is positive.

Tendonitis causes pain on resisted movement involving the specific muscle. Anteromedial pain worsening on exercise and tenderness over adductor region which worsens on resisted adduction points to adductor tendonitis. Lateral pain worsened by resisted abduction points to gluteal tendonitis.

Neurological causes of pain must be looked for. Note if coughing exacerbates the pain on the anterior aspect of thigh and movement of the back worsens this pain. Presence of these features should suggest nerve root compression. The femoral nerve is put to stretch by flexing the knee with patient lying prone. This leads to pain in the L2, L3 distribution if these segments are affected. Likewise stretch on the sciatic nerve elicited by straight leg raising test leads to pain posteriorly in the thigh and leg in lesions of L4, L5 and 51 segments. Pain over the lateral and anterior aspects of the thigh which tenderness over the medial aspect of anterior superior iliac spine occurs in *meralgia paresthetica* caused by compression of the lateral cutaneous nerve of thigh. Before leaving the thigh, check femoral artery pulsation. Look for varicose veins, with the patient in the standing position.

Knee Joint

This joint is examined to give the following information:

1. Assessment of tibiofemoral and femoropatellar joints movements.
2. Detection of deformities
3. Detection of bursitis
4. Assessment of the condition of the entheses, ligaments and menisci, and
5. Ruling out any cause for referred pain.

Inspect the areas around the knee for scars, sinuses and deformities. Note if swellings obliterate

the normal hollows around the knee. Palpate and check for warmth and tenderness. Localized pain and swelling with tenderness confined to the antero-inferior part of the patella indicates ***prepatellar bursitis***. Tenderness and swelling at the insertion of quadriceps tendon occurs in ***infrapatellar bursitis***. Check tenderness over femoral and tibial condyles, anterior surface of patella, medial and lateral joint lines, fibular head and tibial tuberosity. Note if there is tenderness over entheses. Joint effusion presents a horse-shoe-shaped swelling situated anteriorly. Presence of fluid can be confirmed by pushing fluid from the suprapatellar bursa into the joint and tapping on patella. It hits the femur and springs back. This phenomenon is called ***patellar tap*** (Fig. 19.35). If the amount of fluid in the knee is small, patellar "tap" can be elicited only in the standing position.

Now make the patient lie prone. A vague ill-defined tender swelling behind the knee occurs in posterior bursitis. If an obvious swelling is present, flex the knee to relax popliteal fascia and palpate for cystic masses. ***Baker's cyst*** is a cystic cavity communicating with the joint space. Rupture of Baker's cyst causes severe pain and tenderness in this region and diffuse swelling appears between the heads of the gastronemius. When dealing with any popliteal swelling, check if it is pulsatile. Popliteal artery aneurysm presents as a pulsatile mass in this region occasionally.

Tibiofemoral joint disease is indicated by effusion, limitation of flexion and tenderness along the joint line. Patellofemoral lesions cause anterior pain, pain on contracting the quadriceps, tenderness on pressure over patella and often crepitus on grinding patella over femur.



Fig. 19.35: Demonstrating knee joint effusion (Patellar tap)

To test if cruciate ligaments have been injured, check by passive movement if there is an increased anterior or posterior mobility of the leg with the knee kept in 90° flexion. Try to bend the knee outwards and rotate externally keeping the joint 90° flexed. This brings the medial meniscus between femur and tibia. If it is torn, it causes a click or sharp pain. Likewise the condition of the lateral meniscus is checked by inward bending and internal rotation of the knee.

In knee joint disease, flexion deformities develop early. ***Genu recurvatum*** is hyperexten-sion of the knee. In ***genu valgum*** or knock knee, the knee joints are displaced medially, the thigh and the leg form an obtuse angle laterally. In ***genu varum*** or bow legs, the knee joint is displaced laterally, the thigh and leg are bent like a bow with the convexity pointing outwards. All these defects are usually developmental or acquired in diseases such as rickets.

The distance between medial malleoli of tibia when the limbs are kept together straight, gives an indication of the severity of knock knees. Likewise, the intercondylar distance assesses severity of bow legs. If the deformities are due to bending of the femur and not due to knee joint involvement, they disappear when the knee is fully flexed.

Lesions in other joints especially the hips and lumbosacral spine may manifest as pain radiating to the ipsilateral thigh and knee. Therefore it is important to examine the hip and spine particularly before concluding the physical examination. Spinal root compression commonly caused by intervert-ebral disc prolapse leads to pain radiating to the lower limbs.

Compression of L4 dorsal nerve root give rise to pain radiating to the thigh and knee. The pain is aggravated by movement of the back coughing and sneezing. Knee jerk is abolished. Stretch on the femoral nerve aggravates the pain.

Ankle and Foot

Inspect the ankle and foot for deformities. Look for abnormalities of the arch of the foot such as pes planus (flat foot) or accentuated plantar arch (pes cavus), callosities, neuropathic ulcers, inter digital fungal infection and other abnormalities. Filarial edema and elephantiasis leading to gross deformities are common in many parts of India. Destruction of

several tissues in the foot and chronic discharging sinuses occur in Madura foot—*maduramycosis.*

The term ***talipes*** (club foot) denotes deformity of the foot, usually congenital, or at times acquired. ***Talipes equinus*** is extension of the foot in which the person has to walk on his toes. ***Talipes valgus*** is the condition in which the heel is turned outwards. In ***talipes varus,*** the heel is turned inwards.

Arthritis of the ankle causes diffuse pain on standing, worsened by plantar and dorsiflexion of the foot.

Talipes valgus may be due to talonavicular disease. Affection of midtarsal joints causes collapse of the longitudinal arch. In rheumatoid disease, hammer toes occur in which the proximal phalanx subluxes upwards displacing the fibrofatty cushion that normally protects the metatarsal head. This increases load on the metatarsal head and painful callosities develop.

Joints of the foot: Next, flex the ankle and rock the heel from side to side: pain indicates subtalar joint disease (Figs 19.36A and B). Walking on irregular surfaces may be painful.

Fix the hindfoot and twist the forefoot, if there is pain, it suggests midtarsal joint disease. Swelling may also be present (Figs 19.37A and B).

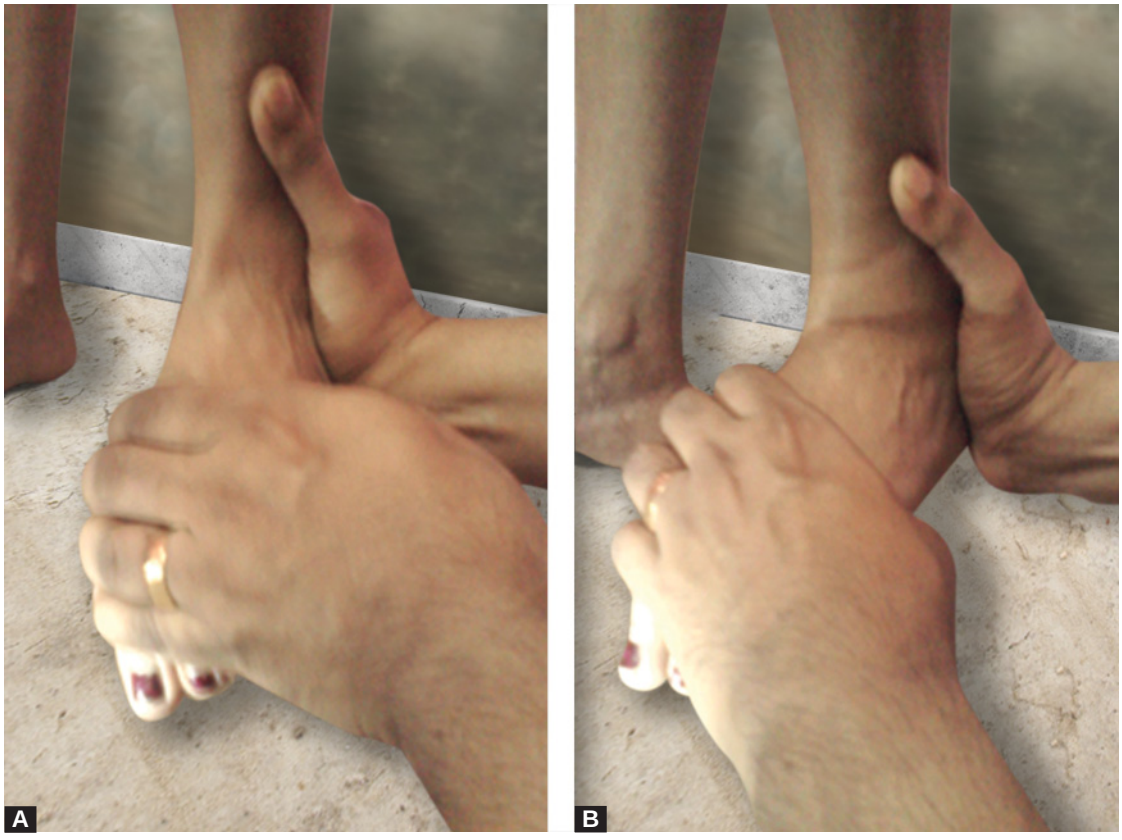
Note if the toes have been pushed apart by swelling near metatarsal heads (day light sign). Compress the metatarsal arch transversely and squeeze individual joints. Pain caused by these maneuvers suggests metatarsal joint disease. Check the toes for tenderness over the interphalangeal joints.

Tendonitis: Note, if the there are swellings related to the peroneal, tibialis posterior and Achilles tendons. Pain localized behind the lateral malleolus with linear swelling along the tendon sheath occurs in inflammation related to the peroneal tendon. Plantar flexion causes pain and inversion worsens it. Likewise linear swelling behind the medial malleolus with pain exacerbated by plantar flexion and eversion suggests inflammation of the tendon sheath of tibialis posterior. Note if there is a diffuse painful swelling behind the ankle which worsens on walking or pressure from footwear; this occurs in Achilles tendon sheath inflammation (Fig. 19.38).





Figs 19.36A and B: Rocking the heel from side to side to elicit subtalar joint tenderness



Figs 19.37A and B: Twisting the forefoot to elicit pain of midtarsal joint disease



Fig. 19.38: Achilles tendinitis

In sub-Achilles bursitis, the pain is similar but the swelling bulges out on either side of the Achilles tendon. Plantar flexion worsens the pain of bursitis. However if plantar flexion is attempted against resistance, there is no worsening of pain in bursitis, whereas in tendonitis pain is worsened.

Move on to the plantar surface. Tenderness under the heel at the insertion of plantar fascia occurs in plantar spur (**calcaneal spur**) and **plantar fasciitis**. Pain and swelling situated more anteriorly over the metatarsal heads should suggest **metatarsal bursitis** (Figs 19.39 and 19.40).

Neurological Causes of Pain in the Feet

The lower limbs are common sites for referred pain due to lesions in the lower segments (L5–S4) of the spinal cord and the corresponding nerve roots. Careful neurological examination is required to reveal the abnormalities. Referred pain manifests as pain and paresthesia in the heel and lateral aspect of the foot. Check for wasting of calf muscles. Weakness of plantar flexion, loss of ankle jerk and diminution of pain sensation over the sole of the foot suggests S1 root lesion. In L5 lesion dorsiflexion of the foot and toes are weak. Sensory abnormality over the medial aspect of the dorsum of the feet may be present. Straight leg raising test may also cause



Fig. 19.39: Sensory loss from compression of common peroneal nerve at knee



Fig. 19.40: Sensory loss from compression of tibial nerve at ankle

pain. A common cause for S1 root compression is intervertebral disc prolapse.

Entrapment of posterior tibial nerve in the tarsal tunnel causes burning sensation in the foot, usually worse at night. Tapping behind the medial malleolus may reproduce symptoms. Sensation of pain may be diminished over the sole of the foot.

Palpation of dorsalis pedis and posterior tibial arteries of the foot should be done to detect vascular occlusion.

Involvement of Other Systems

Rheumatological diseases lead to manifestations in other systems. Full examination of the other systems may be rendered difficult on account of deformities.

Appendix-1 gives range of movement of normal joints.

Appendix-2 gives scheme for rapid clinical examination of locomotor system and recording.

APPENDIX-1

Range of Movement of Normal Joints

Joint	Range of movement
• Cervical spine	: 45° of flexion, extension, lateral flexion, rotation
• Shoulder	: 180° abduction: 50° adduction: 160° flexion: 60° extension: 70° rotation (internal and external)
• Elbow	: 160° flexion: 5° extension
• Radioulnar joints	: 90° pronation and supination
• Wrist	: 70° palmar and dorsiflexion, 25° side-flexion
• Metacarpophalangeal joint	: 90° flexion: 25° hyperextension
• Proximal interphalangeal joints (PIPJ)	: 120° flexion
• Distal interphalangeal joints (DIPJ)	: 80° flexion, 10° hyperextension
• Hip	: 30° extension: 135° flexion: 45° abduction: 15° adduction: 45° rotation (internal and external)
• Knee	: 130° flexion
• Ankle	: 30° dorsiflexion: 45° plantar flexion
• Subtalar joint	: 5° inversion: 5° eversion
• Midtarsal joint	: 35° inversion: 25° eversion
Toes	
• Metatarsophalangeal joints	: 40° flexion, 40° extension
• PIP joints	: 40° flexion
• DIP joints	: 50° flexion

APPENDIX-2

Scheme for Rapid Clinical Examination of Locomotor System and Recording

History taking: Points to ponder

1. Basic information: Age, sex, occupation.
2. Chief complaint
 a. Duration?
 b. Onset? (sudden, gradual, time of day)
 c. Precipitating factors:
 - Infection-sore throat, urethral discharge, septic lesions such as boils
 - Unusual sexual exposure
 - Travel outside native place
 - Contact with infectious diseases
 - Trauma, excessive or unusual activity
 - Drugs, vaccination, injections, surgery
 - Excess of food or alcohol
 - Exposure to sunlight or cold
 - Emotional stress.
 d. Pattern of joint involvement:
 - How many joints?
 - First joint or joints affected
 - Subsequent joints affected
 - Pattern of development: Episodic, migratory, additive, simultaneous
 - Symmetry or asymmetry
 - Severity—worst affected joints or joint.
 e. Time pattern
 If symptoms are persistent:
 - Related to time of day
 - Night pain and interference with sleep
 - Morning stiffness

 If symptoms are episodic:
 - Frequency, regularity, duration of episodes.
 f. Aggravating and relieving factors:
 - Effect of rest and exercise, activity, immobility and treatment.
 g. Resultant problems:
 - Extent of disability: Note ability to carry out essential tasks of daily living, such as washing, bathing, eating, toilet activities, walking, sitting and standing, climbing stairs and others.
3. Associated symptoms:
 a. General: Malaise, fatigue
 b. Specific: Fever, rash, diarrhea, urethritis, and other abdominal symptoms, weight loss, pain elsewhere, symptoms referable to other systems.
4. Pastmedical history
 - Rheumatic fever
 - Tuberculosis
 - Psoriasis
 - Arthritis in childhood.
5. Family history
 - Enquire particularly for ankylosing spondy litis, psoriasis, Behcet's disease, gout, rheumatoid arthritis, ulcerative colitis and Crohn's disease.
6. Social, psychological and domestic details
 - Work and home circumstances
 - Unusual or deficient diet
 - Possible contributory emotional and social problems
 - Mental attitude
 - Motivation.
7. Drugs and other treatments
 - Present treatment for arthritis, dose and regime
 - Past-treatment: Benefit–side effects– outcome (if stopped, why?)
 - Drugs for other diseases.

Physical Examination

1. General
 - Appearance: Well or ill?
 - Obvious diagnosis such as myxedema or acromegaly
 - Pallor, pigmentation and skin rashes
 - Posture
 - Gait.
2. Examination of joints
 a. Inspection
 - Overlying skin: Color and consistency (smooth, shiny, etc.)
 - Resting position
 - Deformities.
 b. Palpation
 - Warmth
 - Nature of swelling: Effusion, soft tissue or bony swelling
 - Tenderness, Localization and severity.

c. Active movement
 - Range
 - Pain
 - Crepitus
 - Stability
 - Deformities correctable.

d. Passive movement
 - Range
 - Pain
 - Crepitus
 - Other abnormalities.

3. Soft tissues
 - Muscle: Power, wasting, tenderness
 - Tendons: Palpable abnormalities—thickening, localized swelling, tendon sheath swelling, tenderness, crepitus
 - Functional abnormalities—triggering, rupture
 - Bursae: Swelling, tenderness, signs of inflammation.
 - Ligaments: Tenderness, stability.
4. Nodules: Tophi, rheumatoid nodules, rheumatic nodules.
5. General examination look particularly for:
 i. Extra-articular features: Pallor, peripheral neuropathy, lymphadenopathy renal disease, and others.
 ii. Rashes: Look at hands for vasculitic lesions, purpura, erythema nodosum, malar rash or discoid rash. Look for psoriatic patches over concealed areas of skin and over the nails. Look for rashes of infections like secondary syphilis.
 iii. Finger clubbing and other evidences of malignant disease.
 iv. Temporal arteritis—palpate over the temporal arteries.
 v. Evidence of local or systemic infections.
6. Other systems: Hepatosplenomegaly, pleural effusion, interstitial lung disease, neurological deficits, valvular lesions, pericardial effusion.

Note: For many of the rheumatological disorders criteria have been laid down by the rheumatism associations of different countries including the Indian Rheumatism Association and these help to establish the diagnosis with certainty when the clinical features overlap.

CHAPTER

20 Investigations in Rheumatology

KV Krishna Das, Binoy Paul

Laboratory investigations, Blood, Synovial fluid examination, Determination of HLA status, X-ray examination, Other imaging techniques, Arthroscopy, Synovial biopsy

LABORATORY INVESTIGATIONS

There are many laboratory tests available for the diagnosis of rheumatological disorders, but no single laboratory marker has proved sufficiently reliable, sensitive or specific to be used in ***isolation***. The diagnosis always depend on the symptoms and clinical signs in combination with the laboratory tests.

BLOOD

Acute Phase Reactants

Acute phase response is a major pathophysiological phenomenon which accompanies inflammation resulting from tissue damage. Acute phase reactants get altered both in acute and chronic inflammation. The major acute phase reactants are ESR, CRP and plasma viscosity.

Erythrocyte Sedimentation Rate

Normal value is up to 10 mm/hr in men and 20 mm/hr in women. Rise in erythrocyte sedimentation rate (ESR) suggests inflammatory processes. Levels above 100 mm/hr should suggest rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), tuberculous arthritis, and polymyalgia rheumatica/giant cell arteritis. ESR is raised in a wide range of diseases and therefore, the test is nonspecific for diagnosis. In many cases, the level of ESR may reflect the severity of the inflammatory process and this can be used as an easily available laboratory parameter for follow-up of the diseases, provided there are no coexisting conditions which modify the ESR. Joint manifestations caused by allergic processes and osteoarthritis are not accompanied by high rise in ESR. In many instances, the intensity of the pathological process and the rise in ESR do not go hand in hand.

The disadvantages of ESR is affected by age and gender, by red cell morphology and numbers, and according to the levels of many kinds of plasma proteins all of which are not acute phase reactants.

C-Reactive protein (CRP): CRP is a beta-globulin present in serum, capable of reacting with the outer coat of pneumococci. Normally, it is absent from human plasma. When inflammatory processes occur in any part of the body, the liver produces an identical protein which can be detected by a slide test using readymade reagents. This test is also nonspecific. The test can be performed quickly within five minutes. CRP is unaffected by age or gender and reflects the value of a single acute phase protein. It is more expensive than determining ESR. Advantages of study of CRP are:

1. Shorter time to perform.
2. CRP is positive even before the ESR starts rising.
3. CRP can be quantified by determining dilution titers.
4. It helps to distinguish between rheumatoid arthritis (RA) and SLE. In RA, CRP is elevated, whereas in uncomplicated SLE, ESR will be normal.

Routine Blood Counts

Hemoglobin and Erythrocyte Count

Reduction of hemoglobin level is seen in chronic rheumatoid disease. This anemia may be due to impairment of utilization of iron, hemolysis, or toxic effects of antirheumatic drugs. SLE may be associated with hemolytic anemia.

Leukocyte Count

Total leukocyte count (TLC) is elevated in the acute phase of inflammatory arthritides. Considerable elevation of TLC with marked preponderance of neutrophils suggest septic arthritis, acute rheumatoid disease or acute gout. In chronic forms of these diseases and in tuberculous arthritis, lymphocytes may show relative preponderance. TLC and differential count are absolutely essential to diagnose acute leukemia which may masquerade as poly-arthritis on initial presentation.

Platelet Count

Generally, platelet count is not diagnostic of the primary condition. Thrombocytopenia may occur in SLE as part of the disease. More often thrombo-cytopenia is an early sign of drug induced bone marrow aplasia. Several drugs such as the NSAIDs, methotrexate, and cyclophosphamide are known to produce bone marrow aplasia.

Serological Tests

Serological tests to detect several immune markers in the serum of patients with poly, pauci and mono-arthritis are employed almost universally for the diagnostic work-up, assessment of prognosis and follow-up of response to therapy. Several markers are available for diagnostic work-up.

Rheumatoid Factor

Presence of rheumatoid factor (RF) can be detected by several tests such as sheep cell agglutination test (Rose-Waaler), latex fixation test and nephalometry. The latter are easier to perform since commercial kits are available and, therefore, they are more popular. Rheumatoid factor (RF) which consists of different types of immunoglobulins is present in 70 to 80% of cases of rheumatoid arthritis (RA). Since, the usual tests detect only IgM antibodies, negative results are obtained in about 25% of cases. The presence RF has assumed great importance so that RA can be broadly divided into seropositive and seronegative groups. Presence of RF has been associated with poor prognosis.

Presence of RF is not specific for RA. Other conditions in which RF is present in a smaller proportion of cases include SLE, progressive systemic sclerosis, mixed connective tissue disease and others. False positive RF may be seen in several other conditions such as infective endocarditis, leprosy or tuberculosis. If RF is present in high titers (above 1/40) and the clinical points favor a diagnosis of RA, the test can be taken as diagnostic.

Antibodies to Cyclic Citrullinated Peptides (Anti-CCP)

This is a new antibody test for the early diagnosis of RA. Citrulline is found in synovial joints of rheumatoid arthritis patients. Formations of anti-cyclic-citrullinated-peptide (anti-CCP) antibodies is specific for RA patients. Test for anti-CCP antibodies have been refined. The initial test was anti-CCP_1 assay. The present one is anti-CCP_2 assay which performs better. These are antibodies to cyclic citrullinated peptides which are highly specific for RA (96% specific, 70% sensitive) these antibodies are present early in RA patients even before developing arthritis.

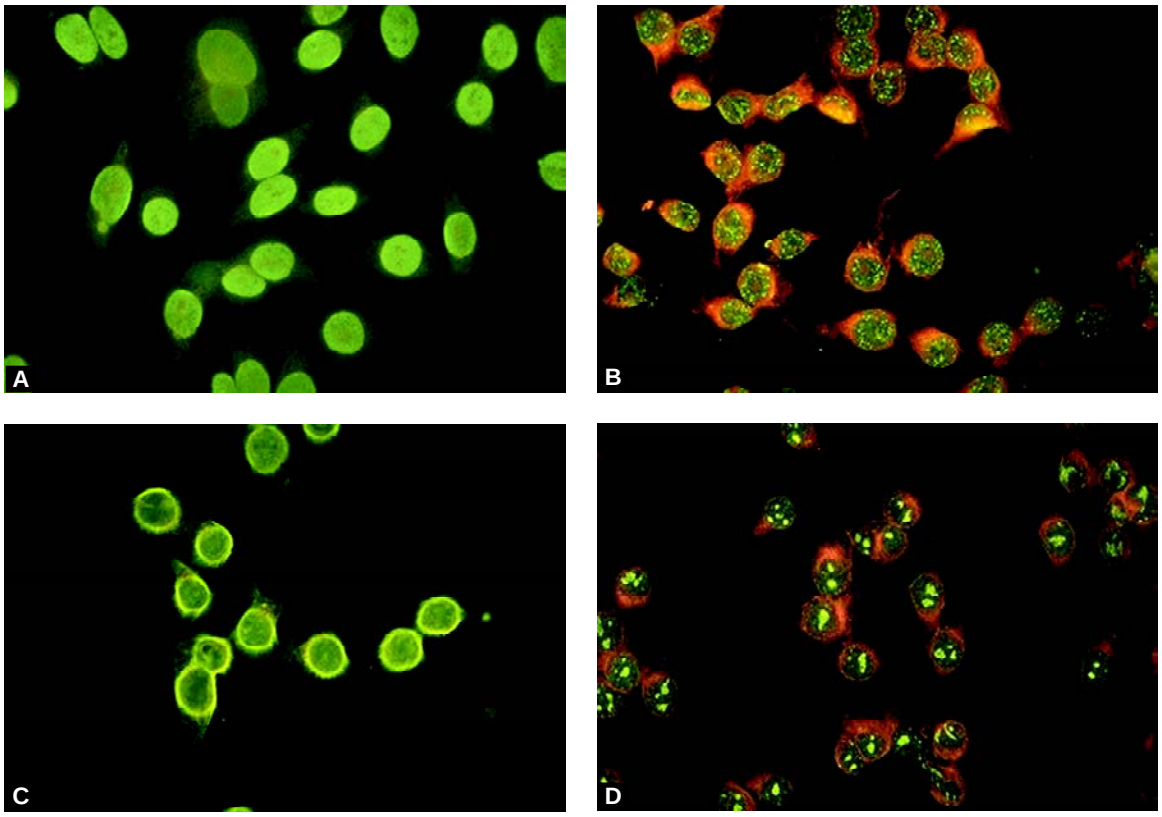
High titer also correlates with erosive changes in bone.

Anti-Streptolysin O (ASO) Titer

This is an easily performed slide test. Positive tests with titer above 1/200 Todd units indicate recent streptococcal infection. Rising titers are more reliable. Presence of ASO, alone does not confirm the diagnosis of rheumatic fever unless the clinical setting is appropriate. Streptolysin is one of the components of streptococcal antigens. Antibodies formed against streptolysin (antistreptolysin O) is another marker of recent streptococcal infection.

Antinuclear Antibodies

These are present in many of the connective tissue diseases. For the sake of convenience certain anticytoplasmic antibodies are also clubbed with the antinuclear antibodies (ANAs) as they have a similar role in pathogenesis in these diseases. Auto-antibodies in serum can be detected by flocculation tests, immunohistochemistry, radioimmunoassay,



Figs 20.1A to D: Fluorescent antinuclear antibody patterns: (A) Homogeneous pattern—dsDNA; (B) Speckled pattern—Sm, SnRNP, Ro,La; (C) Rim pattern—dsDNA; (D) Nucleolar pattern—scl-70, SnRNP

immunodiffusion or immunoblotting. Immunohistochemistry can be done by indirect immunofluorescence (IIF), enzyme linked immunosorbent assay (ELISA) or radioimmunoassay (RIA). The IIF is most commonly used to detect ANAs. The patient's serum is mixed with cultured cells which have the concerned antigen. If the patient's serum has the antibody, it binds to the antigen. Excess antibody is washed away and the antibodies bound to the cell are detected by using a second antibody which is labeled. Excess of second antibody is washed away and the fluoresence is measured. In addition to detection of ANAs they can also be quantified. ANAs associated with different diseases often react in different patterns giving further clues to the diagnosis (Figs 20.1A to D). A diffuse homogenous nuclear pattern detects antibodies to dsDNA and suggest SLE. A speckled pattern occurs in Sjögren's syndrome and mixed connective tissue disease. A nucleolar pattern occurs often in scleroderma. A peripheral pattern also occurs typically in SLE.

Different autoantibodies are seen in different connective tissue diseases (Table 20.1). Specific antibodies to double stranded DNA (dsDNA) and single stranded DNA (ssDNA) are seen most commonly in SLE. Antibodies to dsDNA are seen particularly in SLE with nephritis and CNS involvement and the titers fall as the disease activity comes down. As the disease improves anti-dsDNA titers falls. These antibodies are usually absent in drug induced lupus and discoid lupus. Specific antihistone antibodies are almost always present in drug induced lupus. This can be used as a reliable screening test to detect drug induced lupus at an early stage in patients receiving drugs such as phenytoin, hydralazine or INH.

Anticentromere antibodies: Occur in scleroderma, and CREST syndrome nonhistone nuclear proteins can be extracted as they are soluble and hence they are called extractable nuclear antigens. These are detected by immunodiffusion or immunoblotting. **Antibodies to Smith antigen** (Anti-Sm) are specific for SLE. **Antibody to RNP** was thought to be specific for mixed connective tissue disease (MCTD), but now it is clear that many of these

patients also progress to develop rheumatoid arthritis or scleroderma. **Antibodies to SS-A (anti-Ro)** are seen in SLE and Sjögren's syndrome. Antibodies to an antigen named **Scl-70** are seen in scleroderma and antibodies to JO-1 are seen in polymyositis. It must be remembered that overlap does occur and therefore, a firm diagnosis should take into account the clinical features, immunological markers and other investigations.

Antineutrophil Cytoplasmic Antibodies

Antibodies to cytoplasmic antigens which develop in several forms of vasculitides are employed for diagnosis. The most important ones are *anti-neutrophilic cytoplasmic antibodies (ANCA)*. These are IgG antibodies. When they react with proteinase 3, present in the cytoplasm of neutrophils they are called cytoplasmic ANCA (c-ANCA).

When the reaction is perinuclear, it is called p-ANCA. When the staining is atypical, it is called a-ANCA. c-ANCA is specific for Wegener's granulomatosis p-ANCA is more characteristics of vasculitides such as Churg-Strauss syndrome, polyarteritis nodosa and idiopathic crescentic rapidly progressive glomerulonephritis (RPGN). p-ANCA and a-ANCA may be positive in a variety of conditions such as glomerulonephritis, systemic lupus erythematosus, rheumatoid arthritis, polyarteritis nodosa, ulcerative colitis, Crohn's disease, tuberculosis, HIV infection and others.

Antiphospholipid Antibodies

These are directed against negatively charged phospholipids. These include anticardiolipin antibodies and circulating lupus anticoagulant. Lupus anticoagulant is directed against the coagulation factors X and V and the platelet phospholipids. The presence of these antibodies has been linked to a syndrome known as the *antiphospholipid antibody syndrome* characterized by recurrent multiple arterial and venous thrombosis leading to transient ischemic attacks, cerebrovascular accidents, myocardial infarction, recurrent abortions, thrombocytopenia and livedo reticularis in the skin. The antiphospholipid antibody syndrome (AP/AS) may occur as a primary condition or it may be seen also in other connective tissue diseases. The lupus anticoagulant is detectable in 30% of systemic lupus erythematosus. ***Among clinically normal individuals tests for these antibodies may be weakly positive in a small proportion. Therefore, the significance of the tests has to be correlated with the clinical presentation***.

Serum Complement Levels

Components of the complement system such as C3 and C4 are consumed during antigen antibody reactions occurring in collagen vascular diseases. Elevated titers of anti-dsDNA antibodies are typically accompanied by hypocomplementemia. Reduction in levels of C3 suggests active SLE.

Demonstration of LE Cell Phenomenon

Presence of LE cells is suggestive of SLE. The LE cells can be demonstrated in active SLE. The LE cells are also rarely seen in RA, allergic states, drug induced lupus, etc. Due to low sensitivity and low specificity, it is replaced by ANA in modern laboratories (Fig. 20.2).

Serological tests for syphilis—VDRL: Though syphilitic arthropathy is not very common, syphilis is a curable cause of bone and joint disease. Arthritis may occur in the secondary stage of syphilis. In the tertiary stage gumma may develop. In congenital syphilis, syphilitic epiphysitis may be seen.

Apart from syphilis, false positive VDRL reaction may occur in SLE. With treatment of the primary disorders, the VDRL test also becomes negative. False positive VDRL is more frequently associated with antiphospholipid antibodies.

Serum uric acid: Serum uric acid is raised (normal 5-6 mg/dL) in hyperuricemia and gout. Serum uric acid should be examined after overnight fasting.

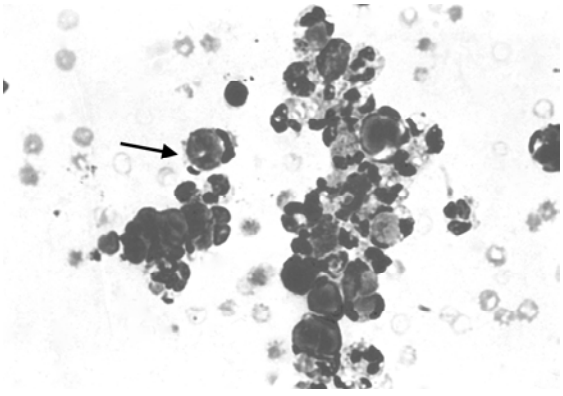


Fig. 20.2: LE cell—a neutrophil leukocyte engulfing amorphous eosinophilic material—its own nucleus pushed to the periphery (arrow)

Table 20.1: Antinuclear antibodies in connective tissue diseases

Antibody	*Disease*	*Comments*
dsDNA	SLE	High specificity, moderate sensitivity
Smb (Smith)	SLE	High specificity, low sensitivity
Ro (SSA)	Skin LE, Sjögren's	Complete heart block in newborn
La (SSB)	Sjögren's, lupus	Minor salivary gland biopsy
snRNP	MCTD	Also seen in SLE, scleroderma, RA
Scl -70	Diffuse scleroderma	Lung involvement in scleroderma
Centromere	CREST syndrome	Also seen in limited scleroderma
Histone	Drug induced SLE	Positive in 100% cases
Jo-1	Dermatomyositis	Low sensitivity

Each laboratory should standardize its results and give its normal values for comparison. Administration of NSAID reduces serum uric acid level. Therefore false negative values may be seen even in gouty subjects receiving NSAIDs. In chronic tophaceous gout, serum uric acid is elevated, often above 8 mg/dL but in acute gout, the serum uric acid may be normal. Moreover all cases of hyperuricemia may not present with gouty arthritis. Table 20.1 summarizes the diagnostic relevance of antinuclear antibodies in connective tissue diseases.

SYNOVIAL FLUID EXAMINATION

Examination of the synovial fluid is a very reliable and cost effective test for diagnosis of joint disease. When the diagnosis is in doubt, this should be done early. It can be done as a bedside procedure. Normal synovial fluid is a thick viscous yellow liquid. Fluid from inflamed joints is thin, watery and opalescent (Table 20.2).

The fluid can be examined as a fresh wet preparation under the microscope after staining with methyline blue. Other tests include cell count, cytocentrifugation to detect microorganisms and culture, and polarized microscopy for crystals.

DETERMINATION OF HLA STATUS

In humans, the short arm of chromosome 6 contains the genes that regulate immunological processes and these are called the major histocompatibility complex (MHC). It extends over about four million base pairs. These code for the HLA proteins which are of two types, i.e. HLA class I antigens and HLA class II antigens. HLA class I molecules are distributed widely among most somatic cells of the body with the exception of erythrocytes. HLA class II molecules are seen mainly in the cells of the immune system such as B-lymphocytes, macrophages, dendritic cells and a groups of T-cells. One of their main functions is concerned with the presentation of antigens to CD4 positive T-cells which activate further immunological processes. Certain HLA types have strong association with different rheumatological diseases. HLA-B_{27} is often positive in ankylosing spondylitis and other seronegative spondyloarthritis. HLA-DR4 may be positive in RA and DR2 or DR3 in SLE.

In routine clinical rheumatological practice only detection of HLA-B_{27} become a standard investigation, due to its very strong association with ankylosing spondylitis. It is not needed in a definite case of ankylosing spondylitis. But HLA-B_{27} is useful in suspected spondyloarthritis, acute uveitis with low back pain and normal X-ray, asymmetrical oligoarthritis or recurrent enthesitis, and in woman with inflammatory back ache and normal radiology.

Table 20.2: Synovial fluid analysis

Feature	*Normal*	*Noninflammatory arthritis*	*Inflammatory (noninfectious) arthritis*	*Infective arthritis*
Volume	< 1 mL	> 1 mL	> 1mL	> 1 mL
Viscosity	High	High	Low	Variable
Color	Colorless	Straw to yellow	Yellow	Variable
Clarity	Transparent	Transparent	Translucent	Opaque
WBC count	< 200/cmm	50-1000/cmm	1000-75000/cmm	>100000/cmm
Neutrophils	< 25%	< 25%	Often> 50%	> 85%
Culture	Sterile	Sterile	Sterile	+
Mucin clot	Firm	Firm	Friable	Friable
Glucose	Nearly equal to blood glucose	Nearly equal to blood glucose	Low (<50 mg%)	Very low (< 20 mg%)
Crystals	-	±	±	-

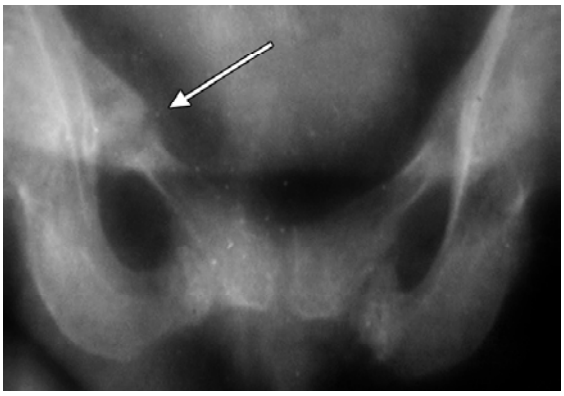


Fig. 20.3: Osteomalacia showing pseudofracture pelvis (arrow)

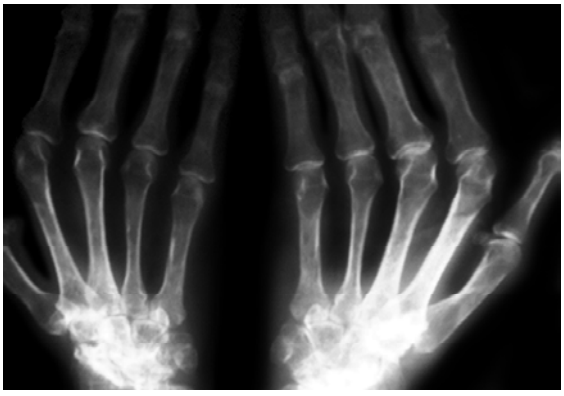


Fig. 20.4: Radiograph of hands in rheumatoid arthritis—periarticular osteoporosis of metacarpophalangeal joints and erosion of proximal interphalangeal joints, destruction of carpal bones and ulnar deviation



Fig. 20.5: Radiograph of foot in chronic tophaceous gout showing punched out lytic lesions with overhanging margins (arrow)

Determination of HLA-B_{27} is also useful to identify persons who may develop ankylosing spondylitis in future.

X-RAY EXAMINATION

This is a very simple, reliable easily available and cheap investigation giving diagnostic information in most of the diseases associated with structural changes in bones and joints. X-ray examination is routinely done in almost all rheumatic diseases for the following purposes:

1. To exclude bony and joint lesions.
2. To establish the diagnosis by the presence of typical changes.
3. To confirm the clinical diagnosis and the stage of disease.
4. For follow-up.

Characteristic abnormalities which are themselves diagnostic occur in osteoarthritis, cervical spondylosis, ankylosing spondylitis, rheumatoid arthritis, gout, tuberculous arthritis, osteomalacia, fluorosis and others. Serial X-rays form the most reliable records for follow-up of the cases (Figs 20.3 to 20.6). In traumatic lesions, skiagrams are mandatory to detect fractures and dislocations.

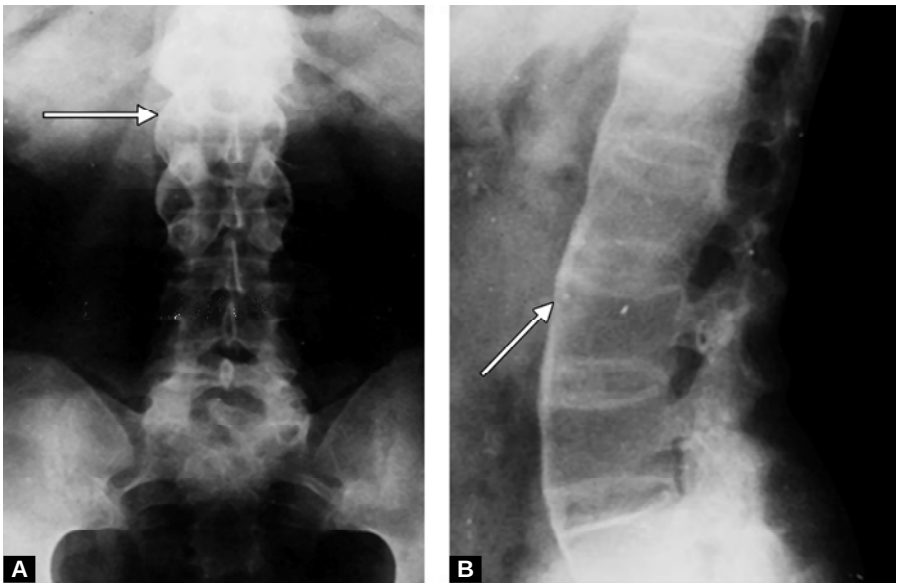
OTHER IMAGING TECHNIQUES

Apart from plain X-ray examination several imaging techniques are available to study bone and joint problems. These may be required at times when other investigations fail to confirm the diagnosis. These include computerized tomography (CT) scan, musculoskeletal ultrasonography, magnetic resonance imaging (MRI), bone densitometry—dual energy X-ray absorptiometry (DEXA) scan and radioisotope bone scintigraphy.

CT scan gives clear pictures of bony abnormalities and soft tissues. Discrimination between bone and joint diseases is generally clear. CT scan and MRI are very useful to pick up sacroiliitis in early ankylosing spondylitis. It detects periarticular and ligamental thickening and calcifications and also detects early changes in bone and adjacent soft tissues.

The indications for CT scan are increasing. Multidetectors CT scanning gives better details and hence this may be done when facilities are available.

Magnetic resonance imaging: This is the ideal imaging for diarthordial joints when diagnostic information cannot be obtained by other modalities MRI can detect pre-erosive inflammatory changes, synovial hyperplasia and joint effusion It is also very



Figs 20.6A and B: X-ray lumbosacral spine—ankylosing spondylitis. *Note:* Calcified ligaments, giving rise to bamboo—spine appearance (arrow)

useful to detect bony erosions early in RA. MRI clearly delineates soft tissue changes like thickening or rupture of tendons, meniscial tear inside the knee joint and others. Changes in the spine and intervertebral disk are also better imaged with MRI. It is also considered as the gold standard imaging of brain in neuropsyciatric lupus and vasculitis. MRI can detect infarcts, hemorrhage, demyelination and vasculitic brain damage.

Early inflammatory changes are picked up on MRI scans before they become evident in conventional X-rays or CT scans. Dynamic contrast enhanced MRI is even more efficient in this respect. Inflammatory changes reflecting active sacroilitis include:

1. Bone marrow edema.
2. Synovitis.
3. Enthesitis.
4. Capsulitis.

Diffusion weighted imaging (DWI) can quantify the diffusion coefficients of lesions which can discriminate between normal and affected sub-chondral bone.

Ultrasonography with high frequency linear probe is useful in diagnosing synovitis, erosions tenosynovitis, tendon rupture or minimal effusion Joint aspiration or injection under ultrasound guidance in sacroiliac joint, hips or shoulders markedly increase the accuracy of the procedure.

Radionucleotide scanning of bone shows areas of increased or decreased activity related to vascularity, metabolism or inflammation of bone and joints. It is very sensitive to changes in tissue activity but highly nonspecific. ^{99m}Tc scintigraphy commonly employed in our country is very useful to detect bone metastasis, occult infections like septic disciitis and stress fractures.

Bone Densitometry

This is the measurement of bone mass or bone mineral density (BMD) which is the most reliable parameter to diagnose osteoporosis and to predict the chances for fragility fractures in future. Several types of bone densitometers are available world-wide. In India, the two types available are ultrasound densitometers and dual energy. X-ray absorption densitometers (DEXA). The latter is more reliable and results are more reproducible, though it is more expensive.

The results of DEXA are quantitative values, expressed in two forms T-scores and Z-scores. T-scores compare the BMD of the patient with the mean peak BMD of the normal young adult population using standard deviation (SO).

Z-score compares the BMD of the patient with the mean BMD of patients of the same age. The sites commonly measured are the lumbar spines (Ll-L4) including the intervertebral disks, hips and

Table 20.3: WHO criteria for osteoporosis in adult women using T-scores by DEXA

Normal	BMD is within 1.0 SD of the young adult reference mean
Osteopenia	BMD 1 to 2.5 SD below the young adult mean
Osteoporosis	BMD more than 2.5 SD below the young adult mean
Severe osteoporosis	Osteoporosis with the presence of one of the fragility fractures

forearm. BMD of any other part of the skeleton or that of the whole skeleton can also be determined (Table 20.3).

ARTHROSCOPY

This is endoscopic visualization of joints though an arthroscope. Arthroscopy is done for biopsy, therapeutic debridement of diseased joint structures, synovectomy and arthroscopic fixation of intra-articular structures following injury, etc. knees and shoulders are the most frequently arthroscoped joints. As a therapeutic measure, it has given the best results in osteoarthritis. Removal of loose bodies and debridement have given significant improvement in joint function and pain reduction. In skilled hands and well chosen cases arthroscopic treatment is very useful to give relief.

SYNOVIAL BIOPSY

It is a useful procedure to make a definite diagnosis of undiagnosed chronic monoarthritis. In conditions like synovial malignancies and tuberculosis it gives a definite diagnosis.

SECTION

8

Hematological System

CHAPTER

21 Hematology: General Considerations

Mathew Thomas, KV Krishna Das

General considerations, Pattern of common hematological disorders in India

GENERAL CONSIDERATIONS

Blood, bone marrow and the lymphoreticular systems constitute hematological organs in the adult.

Embryology

Blood cell production begins in the yolk sac at about day 7 post coitum from the mesoderm and continues till day 12.5 in the mouse. Subsequent research has shown that the first human adult type of hemopoietic stem cells (HSCs) is derived from the mesodermal cells of the aorto-gonad-mesonephros (AGM) region of the embryo particularly from the ventral wall of the dorsal aorta. AGM remains as a source of hematopoiesis between 9.5 to 11.5 days in the mouse and 30 to 37 days in the human. Approximately 2 days following the appearance of HSCs in the AGM region hematopoiesis begins in the liver and it is the major source of hematopoiesis around 5 weeks' gestation. The marrow begins to populate with hematopoietic cells at 8 weeks' gestation. The final shift in the site of hematopoiesis from the liver to bone marrow occurs before birth. It is interesting to note that a large number of HSCs and progenitor cells circulate during fetal life. But the neonatal blood contains less number of progenitor cells because immediately after birth hematopoietic cells begin to home to and lodge in the bone marrow. This marrow localization is found to be dependant on stromal cell derived factor (SDF). The shifts in localization of hematopoiesis is probably due to change in the cell adhesion molecules on the surface of the HSCs and the characteristics of stromal cells in different sites as yolk sac, AGM, liver and bone marrow. In the fetus the hemoglobin is almost totally fetal hemoglobin (HbF) made up of two alpha and two gamma chains ($\alpha 2\gamma 2$) which is best suited to function in the intrauterine environment. Fetal hemoglobin falls to below 2% by the age of six months. Adult hemoglobin (HbA) made-up of two alpha and two beta chains ($\alpha 2\beta 2$) starts appearing in fetal erythrocytes by the eleventh week of gestation and after birth it rapidly replaces fetal hemoglobin.

The total blood volume is about 5 L in the adult (65 mL/kg) made-up of plasma and the formed elements.

The bone marrow is a loosely—knit semisolid tissue contained within the marrow cavity of almost all bones. The total weight of the bone marrow in adult varies from 1600 to 3700 g. Active red marrow constitutes approximately 1000 g. The proportion of active hemopoiesis taking place in different bones is given below:

Pelvic bones	34%
Vertebrae	28%
Cranium and mandible	13%
Sternum and ribs	10%
Scapulae, humeri, and clavicles	8%
Femur	4%

The cellular components of the bone marrow are:

	Mean values
Myeloid precursors and granulocytes	57%
Erythroid precursors	25%
Lymphocytes	16%
Monocytes	3%
Plasma cells	1.3%
Reticulum cells	0.3%
Megakaryocytes	0.1%

In addition, the microenvironment of the marrow where the HSCs are produced and mature is becoming clinically very important. This microenvironment consists of:

1. Stromal cells—fibroblasts (most studied), marrow endothelial cells, osteoclasts
2. Cytokines—stem cell factor (steel factor, c-kit ligand), Flt 3 ligand, thrombopoietin
3. Matrix proteins—fibronectin, hyaluronan, heparan sulphate, tenascin, laminins, collagen.

The effects of the contents of this microenvironment are profound and are being studied in depth. This information is crucial in areas like transplantation, gene therapy and regenerative medicine.

Lymphoreticular organs consist of organized tissues such as lymph nodes, the liver and the spleen. In addition almost all organs contain lymphoid tissue either organized (e.g. thymus, tonsils, adenoids, Peyer's patches in the small intestine and others) or more loosely arranged.

Hematopoiesis and its Regulation

Active production of the formed elements of blood occurs in the cancellous bones and the ends of the long bones. The cells are formed extravascularly in the marrow and they are released into the vascular compartment depending on the demand.

The cells originate from the totipotential hematopoietic stem cells (HSCs). Multipotent progenitors like common lymphoid progenitors and common myeloid progenitors are formed from these cells. Erythroid, myeloid, megakaryocytic and lymphoid precursors are formed by successive differentiation of these multipotent progenitor stem cells. At each stage of differentiation cytokines influence the proliferation and differentiation of the cells. These include predominantly erythropoietin for the erythroid cell lines, colony stimulating factors G-CSF and GM-CSF for leukocytes and thrombopoietin for platelet precursors. Cytokines of lesser role are IL7, stem cell factor (SCF), FLT3 ligand, IL3 and IL5.

Hemoglobin serves the function of oxygen transport. The leukocytes form an important defense against microbial infections particularly the neutrophils against bacteria. Eosinophils play a defensive role against helminthic parasites and in allergic reactions. Though all the functions of the basophils are not yet clear it is known that basophils and tissue mast cells which contain granules rich in histamine play a major role in anaphylactic reactions.

The circulating lymphocyte population consists of T-lymphocytes (80%) B-lymphocytes (15%) and null lymphocytes (5%), T-lymphocytes can further be classified into various subtypes. These take part in cellular immunity. The B-lymphocytes are the main cells concerned with antibody production and humoral immunity. Plasma cells are derived from B-lymphocytes and they actively secrete immuno globulins.

Circulating monocytes have phagocytic activity. In addition, they present the antigens to lymphocytes for further processing. Platelets take part in the initial steps of hemostasis (primary hemostasis), augment the process of coagulation (platelet procoagulant activity) and also help in the final disposal of the clot. In addition to hemostatic activity, platelets are known to have several other functions as well.

PATTERN OF THE COMMON HEMATOLOGICAL DISORDERS IN INDIA

Hematological problems are widely prevalent. Almost all the known hematological disorders have been described from India.

Anemias

Most frequent hematological disorder seen in all communities is ***iron deficiency anemia*** (IDA). It is more prevalent in women and children. The average prevalence in the general apparently healthy population is 7.2% but in particularly vulnerable groups such as agricultural workers and slum-dwellers it may be even over 80%.

Nutritional macrocytic anemia caused by dietary inadequacy of folates and malabsorption states is prevalent more among pregnant women and children. Unlike in the west, pernicious anemia is rare. Vitamin B_{12} deficiency occurs less commonly. When it does so, it is due to dietary causes. Over 30% of anemias show deficiency of two or more haematinic factors.

Hemolytic anemia is common. Sickle cell disease, thalassemias and hemoglobinopathies E and D are widely prevalent. Other hemoglobinopathies occur sporadically. Among the congenital red cell abnormalities, spherocytosis is most common. G6PD deficiency is prevalent widely and this predisposes to hemolysis.

The common acquired hemolytic anemias are malaria, autoimmune hemolytic anemia, transfusion reactions, Rh and ABO incompatibility and secondary to several toxic substances and drugs. Hypoplastic anemias are also frequently seen. Many of them are secondary to drug toxicity, hematological malignancies and chronic renal failure. Hereditary aplastic anemias and primary aplastic anemias form 30 to 35% of the total burden.

Anemia of chronic disease (ACD) has become clinically important in recent years. This type of anemia is common in India also. It is found in chronic inflammatory, infectious or malignant disorders. Iron is available but it can not be utilized for hemoglobin synthesis due to complex mechanisms.

Myelodysplastic Syndromes

Both primary (idopathic) and secondary (therapy related) myelodysplastic syndromes (MDS) present with pancytopenia. About 30 to 40% will progress to leukemia when followed up.

Leukemias

All types of leukemias are seen. In adults chronic myeloid leukemia is the most common (25-30%), followed by acute myeloid leukemia (20-25%) and acute lymphatic leukemia (20-25%). Other types are less common. Chronic lymphatic leukemia is much less common when compared to Caucasian population. In children acute lymphatic leukemia predominates.

Multiple myeloma and other plasma cell disorders are seen not infrequently presenting with a range of symptoms such as anemia, infections, bone pains or fractures.

Lymphomas

All types of lymphomas are common. Non-Hodgkin's lymphoma (NHL) is more frequent than Hodgkin's lymphoma (HL). Many of them are seen in advanced stages with prominent lymphadenopathy and systemic manifestations.

Hemorrhagic Disorders

Purpuras constitute 2/3 of cases and coagulation disorders the rest. Among the purpuras immune thrombocytopenic purpura (ITP) is the most common. Secondary purpuras follow next in frequency.

Henoch-Schönlein Purpura

Anaphylactoid purpura is a common disorder presenting with purpura over the skin and several other internal organs. The main pathology is vasculitis. Renal involvement leads to more severe complications in about 1 to 2%.

Among the coagulation abnormalities, acquired causes such as liver failure, renal failure, disseminated intravascular coagulation (DIC), drug toxicity, viperine snake bites and others are numerically predominant. Hemophilia, von Willebrand's disease and Christmas disease constitute most of the inherited coagulopathies.

Due to widespread use of different systems of medicine and free access to drugs, drug induced hematological disorders are not uncommon. These take the form of agranulocytosis, aplastic anemia, hemolytic anemia, thrombocytopathy and thrombocytopenia. AIDS patients occasionally present with thrombocytopenia, anemia and leukopenia.

Thrombophilic conditions with increased thrombotic tendency are caused by a variety of abnormalities such as protein C and S deficiency, antithrombin III deficiency antiphospholipid antibody syndromes, abnormalities of factor V and prothrombin and several others. These have assumed great importance due to their predilection to cause venous thrombosis, arterial thrombosis and fetal loss in pregnancy.

CHAPTER

22 Examination of Hematological System

Mathew Thomas, KV Krishna Das

History, Physical examination, Involvement of other systems in hematological cases, Systemic complications caused by drugs

HISTORY

Most of the points in history and physical examination which are relevant to diseases of the hematopoietic system have been described in this book under different sections.

The following points in history are particularly important:

Nutrition

Dietary history should be taken in detail. Iron deficiency anemia and nutritional macrocytic anemia caused by deficiency of folate and/or vitamin B_{12} are largely due to inadequate dietary intake of these nutrients. Severe protein deficiency may also give rise to anemia. Dietary articles rich in iron are liver, meat, fresh green vegetables, onions, grapes and jaggery. Rich sources of folic acid include liver, meat, green vegetables and fruits. Food articles rich in B_{12} are liver, meat and other animal products. Dairy products (especially yoghurt and butter milk) supply small amounts of this vitamin. Vegetable sources do not contain vitamin B_{12}. Vitamin C deficiency leads to scurvy in which bleeding is a prominent clinical manifestation. Rich sources of vitamin C include citrus fruits, gooseberries *(amla)*, guava, and sprouting pulses.

Sources of Blood Loss

Nutritional deficiency is often complicated by blood loss. Common sources of blood loss are given below:

1. Hemorrhoids.
2. Excessive menstrual bleeding: Menstrual bleeding occurring for more than four days and more frequently than once a month may be taken as excessive. Normal blood loss during a menstrual period ranges around 60 mL. Anemia produced by excessive menstrual bleeding is more common in peripubertal age group in which the adolescent girl gets excess blood loss without adequate nutritional supplementation.
3. Repeated pregnancies at intervals shorter than three years.
4. Ulcerating lesions of the gastrointestinal tract, e.g. gastric and colonic carcinoma, ulcerative colitis, intestinal tuberculosis, peptic ulceration. Extensive use of antiplatelet drugs, and drugs which cause upper gastrointestinal bleeding such as NSAIDs may lead to minor degrees of GI bleeding over prolonged periods and this can lead to anemia.
5. Heavy infestation by hookworms or whipworms. In many parts of India with improved sanitation the prevalence of soil transmitted helminths have come down. Hookworms especially *Ancylostoma duodenale, Necator americanus* and the whipworm *Trichuris trichiura* which are the main causes of gastrointestinal blood loss have come down.

In addition, lesions such as carcinoma of the stomach, colon and uterus may lead to occult blood

loss and present for the first time as anemia even when the underlying condition remains silent.

In all cases of anaemia, source of blood loss if any, should be identified and corrected to get full relief.

History of Drug Intake

Drug intake

Several drugs lead to toxic damage to the blood components and bone marrow. A few examples are given below:

Agranulocytosis

Analgesics—amidopyrine, phenylbutazone, antirheumatic drugs, chlorpromazine, antithyroid drugs like thiouracil and carbimazole.

Aplastic anemia: Chloramphenicol, phenylbutazone, other antirheumatic drugs, gold compounds, arsenicals.

Thrombocytopenia: Antimitotic drugs, sedormid, quinine, quinidine, heparin.

Thrombocytopathy: Aspirin, penicillin, carbenicillin, nonsteroidal anti-inflammatory drugs, amytryptyline, chlorothiazide, tolbutamide, gold, diphenylhydantoin, all antiplatelet drugs given therapuetically. *Extensive use of antiplatelets drugs may lead to minor degrees of GI bleeding and can lead to anemia. The other secondary causes of bleeding tendencies include renal failure, consumption coagulopathy, snake envenomation and scorpion stings.*

Defects in coagulation: Anticoagulants such as heparin, phenindione, warfarin.

Hemolytic anemia: Penicillin, alpha-methyldopa, quinidine.

Lymphadenopathy—Diphenylhydration

Though only very few examples are listed above, it should be remembered that no drug is absolutely safe and the causative role of drugs in hematological disorders should be thoroughly looked into.

Fever

This may be the main presenting symptom in conditions such as acute leukemias, lymphomas aplastic anemia, infection after chemotherapy and immunodeficiency. Pel-Ebstein fever is characteristic of Hodgkin's disease though many cases do not have this. Acute hemolytic episodes may be accompanied by fever and rigor. Recurrent infections associated with fever should suggest the possibility of neutropenia, dysfunction of neutrophils or immunosuppressed states. Lymphoma (HD) may present with PUO. Occasionally fever is seen in myelofibrosis and CLL. Night sweats suggest low grade fever and may be observed in lymphoma and leukemia.

Fatigue, malaise and lassitude may be seen in anemia especially iron deficiency and hematological malignancies. Emotional disorders also often give rise to these symptoms.

Symptomatology in Anemia

Patients may complain of pallor or the secondary effects of anemia such as palpitation, exertional dyspnea, headaches, ringing in the ears, syncope, extreme fatigue, disinclination to work or angina on effort. Symptoms are much more prominent in those in whom anemia develops rapidly. In chronic nutritional anemias considerable degree of adaptation may develop and therefore symptoms may be milder. This adaptation is due to the increase of 2,3-bisphosphoglycerate (2,3-BPG formerly known as 2,3-DPG) in red cells which decreases the oxygen affinity and releases more oxygen at the tissue level. Severe anemia leads to cardiac failure which may be the presenting symptom in some cases.

Bleeding Tendencies

Disorders affecting the hemostatic mechanism present with bleeding. Bleeding which may be spontaneous or brought on by trivial trauma should suggest underlying hemorrhagic disorders. In systemic bleeding disorders hemorrhage occurs from multiple sites and is recurrent. In many cases a positive family history may be obtained. Generalized bleeding tendency has to be distinguished from local causes of bleeding such as angiomatous malformation, telangiectasia, chronic granulomas and the like, in which bleeding occurs from the same site all the time.

The primary abnormality may involve the platelets (e.g. thrombocytopenia or thrombocytopathy), blood vessels (e.g. scurvy and senile purpura), or coagulation factors (e.g. hemophilia, Christmas disease and hepatic failure). Superficial bleeding into mucous membranes and skin such as gum bleeding, purpura, ecchymoses, epistaxis, menorrhagia,

hematuria, hemetemesis and melena are more suggestive of platelet or vascular abnormalities. In this group, bleeding from cuts and wounds can be arrested by local pressure. Bleeding into joints and deep tissue spaces are suggestive of coagulation abnormalities. In these, cuts and wounds give rise to prolonged blood loss, not easily controlled by local pressure. If the extravasated blood tends to clot, this may exclude a major coagulation defect. The bleeding tendency may show periodic waxing and waning.

Secondary causes of bleeding tendencies include renal failure, antiplatelet drugs, consumption coagulopathy, snake envenomation and scorpion bites and several others.

Thrombophilia

This term denotes an accelerated tendency for thrombosis which leads to venous and arterial thrombosis with and without thromboembolic complications. The condition may be inherited as in the case of deficiency of protein-C and protein S, factor V Leyden abnormality, antithrombin III (AT III) deficiency and prothrombin mutation (PT 20210 A). Acquired thrombophilia occurs in conditions such as antiphospholipid antibody syndrome, increase in coagulation factors, hyperhomocysteinemia and pregnancy.

Increase in cuagulability with increase in the levels of normal coagulation factors:

Factor VIII > 150 Iu/dL	4.8 fold
Factor IX > 129 Iu/dL	2.8 fold
Factor XI > 121 Iu/dL	2.2 fold
Hyperhomocysteinemia	2.7 fold
Pregnancy and puerperium	2-14 fold

Swellings

Hematological malignancies give rise to enlargement of liver, spleen, lymph nodes and several other tissues. Retro-orbital masses, bone tumors and tumors at different sites are seen in acute leukemias, myeloma, and chronic myeloid leukemia. Enlargement of lymph nodes may be the presenting complaint in lymphomas, chronic lymphatic leukemia and acute leukemias. Cervical, mediastinal, axillary and abdominal nodes are most commonly affected. Gross enlargement of lymph nodes during the course of chronic myeloid leukemia suggests transformation into the blastic phase. Enlargement of mediastinal lymph nodes may give rise to *mediastinal syndrome* consisting of obstruction to lymphatics, veins and trachea caused by pressure at the thoracic inlet. The face is congested and suffused. The jugular veins are prominent and nonpulsatile. Pressure on the cervical sympathetic trunk caused by enlarged lymph nodes may lead to Horner's syndrome, characterized by ptosis (drooping of upper eyelid), miosis (small pupil), enophthalmos (retraction of eyeball) and anhydrosis (absence of sweating) on the same side of the face. In conditions like chronic myeloid leukemia, the patient may complain of abdominal masses, due to enlargement of spleen and liver.

Bone Pain

This is caused by increased pressure of the hyperplastic marrow. This is seen in acute leukemias, multiple myeloma, chronic myeloid leukemia, and hemoglobinopathies.

Jaundice

Hemolytic jaundice is seen frequently in moderate or severe hemolytic anemias. The depth of jaundice depends on the rate of hemolysis and the amount of hemoglobin broken down. The common disorders which produce hemolytic jaundice are hemoglobinopathies, congenital spherocytosis, autoimmune hemolytic anemias, malaria, drug toxicities and others.

Acute hemolytic anemia occurring in the neonates and infants may give rise to kernicterus with resultant neurological complications, e.g. Rh and ABO incompatibilities. Chronic hemolytic anemias are associated with pigment stones in gallbladder and chronic ulcers on the leg. Obstructive jaundice may develop when pigment stones obstruct the common bile duct. In mild hemolytic states and in subjects with very low hemoglobin levels jaundice may not be prominent. In mild or even moderate hemolytic states the bone marrow compensates for the hemolysis by rapid regeneration of the erythroid precursors (compensated hemolytic anemia).

Dysphagia

Dysphagia is a frequent symptom in iron deficiency state (Paterson-Kelly or Plummer-Vinson syndrome). It is felt as a feeling of constriction or presence of a mass at the lower part of the pharynx. It clears up on correction of the iron deficiency state. Carcinoma

in the postcricoid area has been noted as a late complication of this syndrome in 4 to 16% of these patients.

Family History

Several hematological disorders are hereditary. Table 22.1 shows the more prevalent hematological disorders transmitted hereditarily.

In about a quarter of patients with hemophilia and Christmas disease family history may not be forthcoming. In such cases the mutation would have occurred *de novo*.

Symptoms referable to the other systems which suggest an underlying hematological abnormality.

Nervous System

Paresthesia due to peripheral neuropathy: Dysproteinemias, leukemia, myeloma, lymphoma, vitamin B_{12} deficiency, amyloidosis, vincristine and thalidomide therapy.

Weakness of one or more limbs: *Compression* of central or peripheral nervous system as in lymphoma, leukemia, multiple myeloma.

***Proxymal myopathy*:** Hematological malignancies.

***Foot drop*:** Lead poisoning, amyloidosis, autoimmune diseases, vincristine therapy.

***Paralysis*:** Acute intermittent porphyria.

Headache: Anemia, polycythemia, neuroleukemia lymphoma, opportunistic brain infections with malignancies, cerebral or subarachnoid hemorrhage in thrombocytopenia or other bleeding disorders.

Altered consciousness: Leukemia and lymphoma affecting the brain and meninges, infection of the brain, severe anemia (B_{12} deficiency), polycythemia, hyperviscosity, hypercalcemia, glucocorticoid psychosis, acute intermittent porphyria.

Table 22.1: Hematological disorders transmitted hereditarily

Hemoglobinopathies Thalassemias	Autosomal co-dominant
Thalassemias G6PD deficiency	Autosomal dominant X-linked recessive
Hereditary spherocytosis	Autosomal dominant X-linked recessive
Hemophilia and Christmas-disease Glanzmann's thrombasthenia	Autosomal recessive
von Willebrand's disease	Autosomal dominant
Hereditary hemorrhagic telangiectasia	Autosomal dominant

Eyes

Conjunctival plethora in polycythemia, *blindness* in retinal hemorrhage (severe anemia and thrombocytopenia), blurred vision in hyperviscosity syndrome, partial or complete visual loss in central retinal artery or vein occlusion.

Diplopia: Orbital tumors, extranodal lymphoma, extramedullary myeloma, chloroma.

Mouth

Sore tongue: Folate deficiency, iron deficiency, vitamin deficiency.

Gingival infiltration and hypertrophy: Monocytic leukemia.

Macroglossia: Amyloidosis.

Tongue or mucous membrane ulcers: Acute leukemia, severe neutropenia.

Dryness of mouth: Hypercalcemia.

Respiratory

***Cough*:** Mediastinal lymph nodes.

***Chest pain*:** Rib and sternum involvement in lymphoma and myeloma, nerve root compression, herpes zoster, acute chest syndrome in sickle-cell anemia.

Abdomen

Abdominal fullness, premature satiety, belching and discomfort.

Splenic Enlargement—Several Causes

Abdominal pain: Intestinal obstruction (lymphoma), retroperitoneal bleeding, lead poisoning, ileus secondary to vincristine therapy, allergic purpura, acute hemolysis.

Abdominal crises (acute abdomen): Acute intermittent porphyria, sickle cell anemia.

Diarrhea: Vitamin B_{12} deficiency, malabsorption in small bowel lymphoma.

Constipation: Hypercalcemia, vinca alkaloids, thalidomide therapy.

Genitourinary Symptoms

Erectile dysfunction and priapism: Spinal cord or peripheral nerve damage in hematological malignancies and pernicious anemia, leukemia, sickle cell anemia.

Red urine: Acute intravascular hemolysis, myoglobinuria, porphyria, anthracycline and phenazopyridine drugs.

Amenorrhea: Antimetabolites, alkylating agents.

Musculoskeletal System

Backache

Acute hemolytic reactions, involvement of vertebrae and spinal cord in acute leukemia and aggressive lymphoma, myeloma.

Arthritis and Arthralgia

Gout secondary to hyperurecemia (hematological malignancies, MDS, hemolytic anemia, hemochromatosis, hemarthrosis in hemophilia, collagen vascular diseases, ALL.

Shoulder pain: Splenic infarct (left side), gallbladder disease (right side) in hemolytic disease.

Skin and Miscellaneous

Edema: Unilateral in DVT.

Leg ulcers: Sickle cell anemia.

***Skin*:** Dry skin, thin hair, brittle nails in IDA.

Darkening of the skin: Hematochromatosis.

Skin involvement in chronic GVHD.

Cyanosis: Methemoglobulinemia, cryoglobulins or cold hemagglutinins.

Pruritis: Lymphomas, polycythemia, mycosis fungoides.

Infiltrating skin lesion: Leukemia, lymphoma.

Necrotic lesions: Intravascular coagulation, purpura fulminans, warfarin induced skin necrosis.

PHYSICAL EXAMINATION

The following points have to be specially noted in the general examination:

Nutrition and pallor: Particularly important in anemias.

Cyanosis: Met-and sulfhemoglobinemia

Jaundice: Hemolytic states.

Fever: Infection in leukemias, granulocytopenia and aplastic anemia, lymphomas, hemolysis, chronic myeloid leukemia.

Lymphadenopathy: Lymphomas, leukemias. Lymph nodes should be gently palpated by a circular motion of the finger tips slowly increasing the pressure.

Nails koilonychia, ridging, flattening of nails: Iron deficiency state.

***Purpura/ecchymosis*:** Platelet disorders. Palpable purpura—vasculitis.

Cushingoid features: Long-term corticosteroid therapy.

Congestion of conjunctiva and plethoric appearance: Polycythemia.

Generalized pruritis and excoriation of skin: Polycythemia vera, lymphomas, chronic lymphatic leukemia.

Bronzing of skin: Iron overload states.

Chronic leg ulcers: Hemolytic anemias.

Pigmentation of the skin: Megaloblastic anemia.

Systemic Examination

Mouth and throat should be examined carefully. Presence of cheilosis and glossitis suggest nutritional inadequacy and mucosal damage caused by antineoplastic drugs. In iron deficiency anemia the tongue is smooth, pale and atrophic. Tongue is smooth and red in nutritional deficiency. Macroglossia is seen in primary amyloidosis. Gingival bleeding and purpura in the mouth suggest purpuric disorders. The gum is hypertrophied in acute monocytic leukemia. The oral mucosa and tonsillar region are common sites for infection in neutropenic subjects.

Abdominal examination should be carried out with care so that even mild hepatosplenomegaly and lymphadenopathy are not missed. Moderate or gross splenomegaly is found in chronic myeloid leukemia, lymphoma, hemolytic anemia, myelofibrosis and thalassemias. Splenomegaly is very unusual in aplastic anemia and immune thrombocytopenia. Hepatomegaly is common in leukemias and lymphomas, the size being more in chronic leukemias. Abdominal lymph nodes may be frequently palpable in lymphomas and chronic lymphatic leukemia. Polycythemia may be a complication of renal diseases such as hypernephroma, and renal enlargement should be carefully looked for.

Funduscopy

Ophthalmoscopic examination should be routinely carried out since many hematological diseases produce diagnostic findings. Pallor of the disk is

observed in anemia. Hemorrhages and exudates are seen in aplastic anemia, acute leukemias and thrombocytopenic states. Retinal hemorrhage may also occur as a complication of sudden exsanguinating hemorrhage and rapidly developing anemia. Leukemic deposits can be made out in the retina as raised areas with pale centre. Many patients with chronic myeloid leukemia, polycythemia and hyperviscosity states show engorged and tortuous retinal veins which disappear when the condition is corrected. Sausage shaped retinal veins are observed in Waldenstrom's macroglobulinemia. Features of raised intracranial tension including papilledema may develop in neuroleukemia.

INVOLVEMENT OF OTHER SYSTEMS IN HEMATOLOGICAL DISEASES

Nervous System

Cranial nerve paralysis particularly lower motor neuron facial paralysis, features of meningeal irritation, raised intracranial tension and rarely other neurological deficits like hemiplegia and paraplegia may be seen in acute lymphatic leukemia and less commonly in other acute leukemias. Multiple myeloma leads to compression of the spinal cord. Signs of degeneration of the pyramidal tract and posterior columns may be present in vitamin B_{12} deficiency states (subacute combined degeneration). Immunocompromised individuals have a great tendency to develop recurrent herpes zoster lesions. In hemophilia, bleeding into closed tissue spaces may give rise to compressive neuropathies. Peripheral neuropathy may be seen in POEMS syndrome polyneuropathy, organomegaly, endocrinopathy, M-protein and skin changes (POEMS).

Cardiovascular System

Hyperdynamic circulation develops in anemias. Hemic murmurs are ejection systolic murmurs heard best over the pulmonary area. These are transient and may disappear after correction of anemia Cardiomegaly may occur. Progressive anemia leads to congestive heart failure. In severe anemia auscultation over the root of the neck especially on the right side may reveal a continuous venous hum (bruit-de-diable) due to increased flow through the jugular veins. Occlusion of the vein by pressure abolishes the hum. Rapidly developing severe anemia is a cause of angina pectoris even in the young with normal coronary arteries. The cardiovascular features caused by anemia disappear when the hemoglobin level is corrected. Therefore, it is necessary to re-examine the patient after correction of anemia to confirm the presence of organic cardiovascular disease. Hypertension with polycythemia is called Gaisbock's syndrome. Multiple venous and arterial thrombosis may develop in polycythemia and severe thrombocytosis and thrombophilia.

Locomotor System

Arthritis, joint swellings or ankylosis should be looked for. Acute lymphatic leukemia may present with joint symptoms resembling rheumatic fever. Arthropathy may occur as a result of hyperuricemia and secondary gout as occurring in leukemias, myeloma, polycythemia and myelofibrosis. In hemophilia painful swellings of joints develop in the acute phase due to intra-articular bleeding. Recurrent bleeding leads to ankylosis of joints and muscular wasting. In allergic purpura, painful swelling of small and large joints is common.

Bone pain and bone tenderness are common in conditions associated with hyperplastic marrow. Gentle percussion or pressure over the sternum, ribs or pelvic bones can elicit tenderness.

Gonads

The testes may be involved in conditions such as acute lymphatic leukemia and this should be looked for even in the absence of symptoms.

SYSTEMIC COMPLICATIONS CAUSED BY DRUGS

Several chemotherapeutic drugs used in the treatment of hematological malignancies give rise to systemic complications. A few examples are given in Table 22.2.

Patients who are on chemotherapy develop severe immunosuppression which predisposes to the development of opportunistic infections such as disseminated candidiasis, *Pneumocystis jiroveci pneumonia* and the like. Pyogenic infections tend to disseminate and lead to septicemia.

Infections transmitted through blood transfusions such as malaria, hepatitis B, C, D and human immunodeficiency virus are likely to complicate those requiring transfusion of blood and blood products, unless special precautions are taken.

Table 22.2: List of drugs showing complications corresponding to situation in which they are used, respectively

Drug	*Condition for which used*	*Major toxicity in addition to bone marrow aplasia*
Vincristine	Acute lymphatic leukemia and lymphoma	Peripheral neuropathy, myelopathy
Anthracycline antibiotics, e.g. doxorubicin	Leukemias, tumors, lymphomas	Myocardial toxicity leading to cardiac failure
Cyclophosphamide	Leukemias, tumors, lymphomas	Hemorrhagic cystitis
Methotrexate	Leukemias, tumors	Hepatotoxicity, Pulmonary fibrosis, mucositis
L-asparaginase	Acute lymphatic leukemia	Pancreatitis
Busulfan	Chronic myeloid leukemia	Pulmonary fibrosis, skin pigmentation, cataract
Interferon	Chronic myeloid leukemia	Fever, arthralgia psychosis
All-trans-retinoic acid (ATRA)	Acute promyelocytic leukemia	ATRA syndrome with leukocytosis
Anti thymocyte globulin (ATG)	Aplastic anemia	Immunosuppression, anaphylaxis

CHAPTER

23 Investigations in Hematological Disorders

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Hemoglobin estimation, Enumeration of cells, Staining of blood film, Abnormalities of erythrocytes, Reticulocytes, Erythrocytes sedimentation rate, Leukocytes, Platelets, Diagnosis of leukemia, Bone marrow examination, Special investigation of nutritional anemias, Diagnosis of hemolytic anemias, Leukemia's–cytogenetic investigations, Bleeding disorders, Tests for platelet function, Disseminated intravascular coagulation, Investigation in thrombophillia, Diagnosis of multiple myeloma, Investigation for polycythemia

Complete blood count (CBC) is one of the first hematological investigations to be done. In many of the laboratories this is now done by an automated analyzer which gives the result in a short time as a printout. In addition, cell histograms are also available. These automated analyzers have gradually replaced laborious and time consuming manual methods during the past 50 years. Except in one-man clinics or rural laboratories manual methods have gone out of vogue due to the labor involved and chances for errors.

All hematological cases should have the following investigations done:

- *Complete blood count (CBC):* This will include hemoglobin concentration, red cell count, red cell indices, (mean corpuscular volume—MCV, mean corpuscular hemoglobin—MCH, mean corpuscular hemoglobin concentration—MCHC), hematocrit, red cell distribution width (RDW), reticulocyte count, platelet count, platelet distribution width, mean platelet volume and total and differential leukocyte count.
- ESR and C-reactive protein (CRP).
- Well stained peripheral blood smear.

HEMOGLOBIN ESTIMATION

This should be done as part of general investigation in all patients irrespective of the complaint since anemia is very prevalent in many communities in India. Hemoglobin level has to be repeated at periodic intervals to assess the progress of the condition.

The standard procedure to estimate hemoglobin is by cyanmethemoglobin method using international standards and reliable equipment. The accuracy of the instrument has to be checked regularly.

Normal values of hemoglobin for different age groups accepted by WHO are:

Children

- 6 months to 6 years 11 g/dL and above
- 6 years to 14 years 12 g/dL and above
- Adult males 13 g/dL and above

Adult females

- Nonpregnant 12 g/dL and above
- Pregnant 11 g/dL and above

Increase in hemoglobin above 17.5 g/dL in males and 15.5 g/dL in females occurs in polycythemia and hemoconcentration.

ENUMERATION OF CELLS

The errors of manual methods of enumeration of the cells (erythrocytes, leukocytes and the platelets) are minimized by using automated and semiautomated counters. These are now widely used for measuring various blood parameters. Automated counters require only appropriate samples to be fed into them. Newer counters can measure 8 to 20 parameters.

Principle

Automated analyzers count the blood cells based on either electrical impedance or the principle of light scatter. Mathematical results are obtained by the difference in the electrical and light signals generated when different blood cells pass through the sensing zone of the machine.

These machines require specific reagents, generally supplied by the manufacturer. Periodic servicing and regular quality control checks are essential to ensure accuracy and reliability. Though the initial investment in the machine is high the savings in technician's time and reliability have made them cost-effective and popular.

Erythrocytes	Normal	4.5-6.3 x 10^2/L (4.5-6.3 millions/cmm)
	Polycythemia	Above 7 x 10^2/L (7 millions/cmm)
Leukocytes	Normal leukocyte count	4-10 x 10^9/L (4000-10000/cmm)
	Leukopenia	Below 4 x 10^9/L (4000/cmm)
	Leukocytosis	Above 10 x 10^9/L (10000/cmm)
Platelets	Normal count	2-4 x 10^{10}/L (200- 400,000/cmm)
	Thrombocytopenia	Less than 1.5 x 10^{10}/L (150,000/cmm)
	Thrombocytosis	Above 4.5x 10^{10}/L (450,000/cmm)

Leukocytosis may involve any type of cell, but neutrophil leukocytosis is the most frequent.

Neutrophil leukocytosis: Acute bacterial infections, e.g. pneumonia, septicemia, urinary tract infection, acute hemorrhage, hemolysis, chronic myeloid leukemia, polycythemia vera and drugs, e.g. corticosteroids.

Eosinophil leukocytosis: Tropical eosinophilia, asthma, helminthic infections, Loeffler's syndrome, allergic disorders, eosinophilic leukemia, hypereosinophilic syndrome.

Lymphocytosis: Pertussis, infectious mononucleosis, infective hepatitis, brucellosis, tuberculosis, chronic lymphatic leukemia, lymphomas low grade.

Basophil leukocytosis: Chronic myeloid leukemia, ulcerative colitis, myxoedema, polycythemia vera, Hodgkin's disease, basophil leukemia.

Monocytosis: Monocytic leukemia, tuberculosis, syphilis, brucellosis, malaria, lymphomas.

Staining of Blood Film and Examination of the Slide

In all hematological disorders, it is absolutely essential to examine a well stained blood film which should be carried out by the doctor himself if possible.

A uniformly thin blood smear should be made on a slide either using blood from a finger prick or from freshly drawn venous blood. Leishman stain is most commonly used for routine staining of the slide in India. Other stains such as May-Grunwald-Giemsa stain, or Wright's stain are all employed by different laboratories.

Procedure for Leishman staining:

1. Cover the smear with filtered Leishman stain and keep for 2 minutes (this fixes the smear and denatures the cells).
2. Pour tap water (or distilled water) two to three times the volume of the stain and keep for 7 minutes.
3. Pour off the stain, wash in running water, dry and examine as described below.

First the smear is scanned under low power of the microscope to get an idea about the distribution of erythrocytes, total white cell number and distribution, rouleauxing and parasites such as microfilariae, and to select a representative area for further study under oil immersion.

Abnormalities of Erythrocytes

Normal erythrocytes are circular with a diameter of around 7.2 *fL (femtoliter)*. The center is pale. They do not show gross variation in size or shape. Younger forms of erythrocytes (reticulocytes) are larger and the staining is a mixture of red and blue (polychromatophilia).

Variations

Variation in the size of the RBC is called anisocytosis. Size of the RBC is reduced to an MCV of 80 fL (microcytosis) and the cells are hypochromic in iron deficiency anemia and thalassemic trait. In aplastic anemia the size does not vary. Many young forms (reticulocytes) are present in regenerating anemia. Fragmented RBC (schistocytes) and erythroblasts (normoblasts) should suggest hemolysis. In macrocytic anemia the RBCs are large and the color is uniform without the central pallor. The MCV is greater then 100 fL (femtoliter).

The ***red cell distribution width*** (RDW) gives a quantitative ideas of anisocytosis. Red cell distribution width (RDW) is a quantitative estimation of anisocytosis and is computed as the standard deviation (in fL) or as coefficient of variation of red cell size distribution. Automated instruments produce volume distribution histograms which

allow easy recognition of even mild degrees of anisocytosis. Estimation of mean corpuscular volume (MCV) does not give accurate values when the number of macrocytes or microcytes is small. RDW is a useful investigation in such situations. Normal range is 42.5 ± 3.5 fL (standard deviation) or 12.8 ± 1.2% (as coefficient of variation). RDW is used for classifying anemias and as an indicator for morphological analysis in the clinical laboratory. It is elevated in iron deficiency anemia, but not in thalassemias or anemia of chronic disease. It is increased (above 17) in megaloblastic anemia compared to other causes of macrocytosis.

Shape

Normal RBC is circular. Variation in shape is termed poikilocytosis. Erythrocytes are oval in elliptocytosis (Fig. 23.8) and spherical in spherocytosis. Unlike normal RBCs which are biconcave, spherocytes are biconvex and therefore in the film they appear smaller, circular and denser (Figs 23.1 to 23.17).

Other abnormalities in the shape which are less common are the following:

Acanthocytes abetalipoproteinemia:

- Spur cells — Hepatocellular disease
- Burr cells — Renal failure
- Acanthocytes — Abetalipoproteinemia
- Schistocytes — Hemolytic anemia, especially autoimmune hemolytic anemia, and microangiopathy.
- Target cells — Thalassemia and hemoglobinopathies
- Sickle cells — Sickle cell anemia
- Tear drop cells — Myelofibrosis

Color

In iron deficiency anemia and thalassemia traits the RBCs are hypochromic, i.e. an increase in the central pallor. They are normochromic in macrocytic anemia and more dense in spherocytosis.

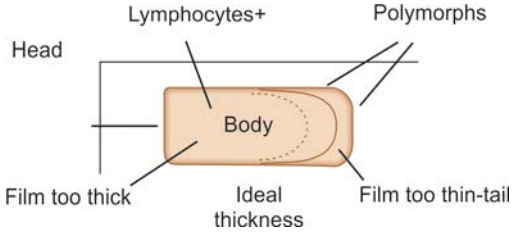


Fig. 23.1: Ideal blood smear

Normal Blood Smear and Pathological Abnormalities of Erythrocytes (Figs 23.2 to 23.21)

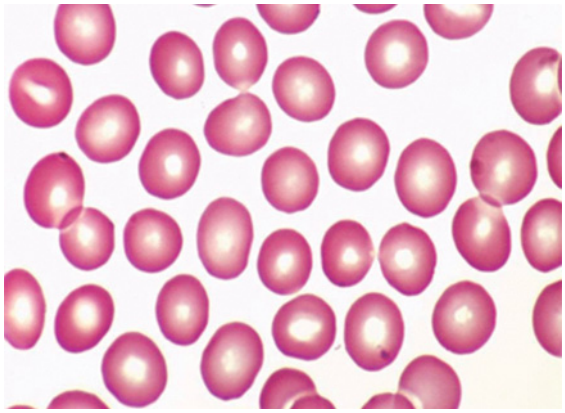


Fig. 23.2: Normal blood smear

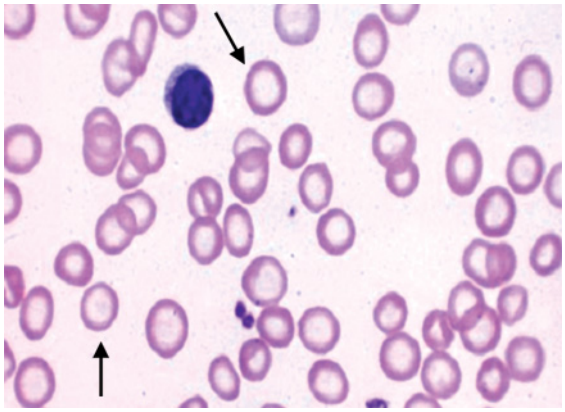


Fig. 23.3: Hypochromic microcytic cells (arrows)

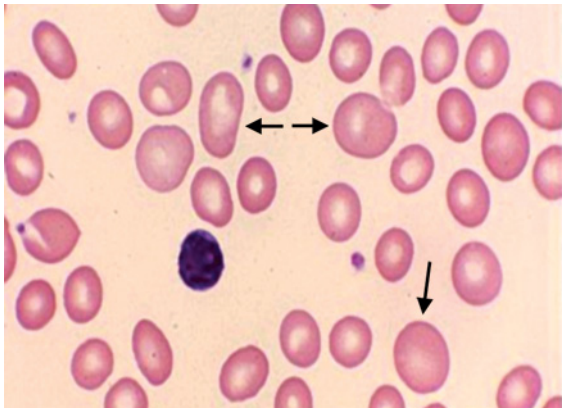


Fig. 23.4: Macrocytes (arrows)

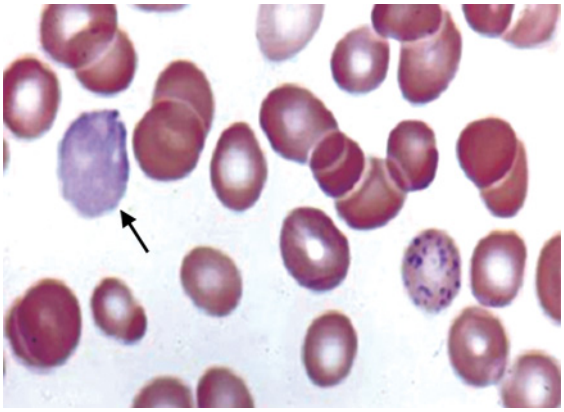


Fig. 23.5: Polychromatophilic macrocyte (arrow)

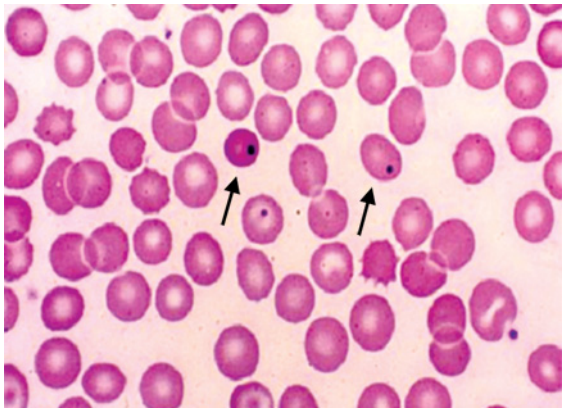


Fig. 23.8: Howell-Jolly bodies—nuclear remnants in the cytoplasm of RBC (arrows)



Fig. 23.6: Punctate basophilia (arrow). Note basophilic granules in the cytoplasm of RBC

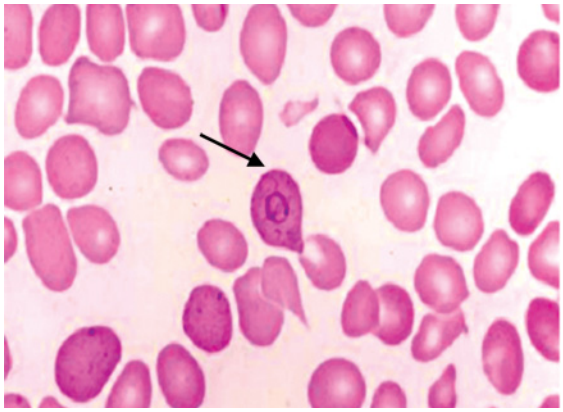


Fig. 23.9: Cabots ring which is remnant of nuclear material (arrow)

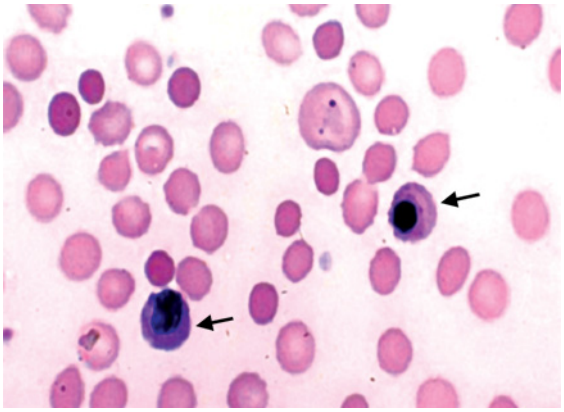


Fig. 23.7: Normoblast—normal precursor of RBC. *Note:* the nucleus and hemoglobinized cytoplasm (arrows)

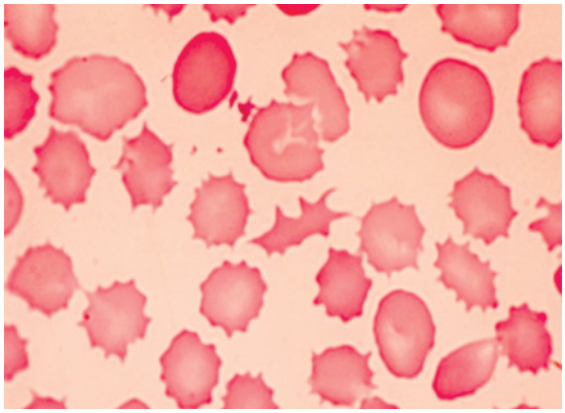


Fig. 23.10: Burr cells—note short spiny margins

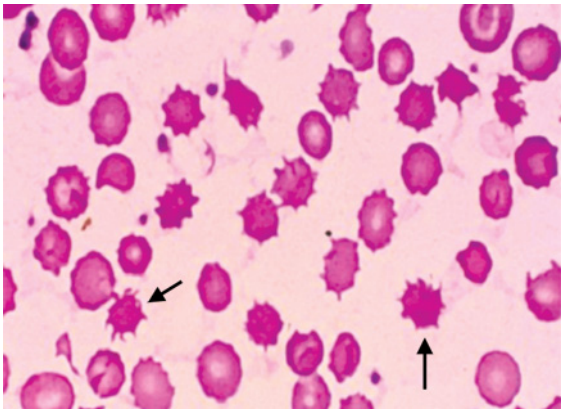


Fig. 23.11: Acanthocytes—note the thorn like projections

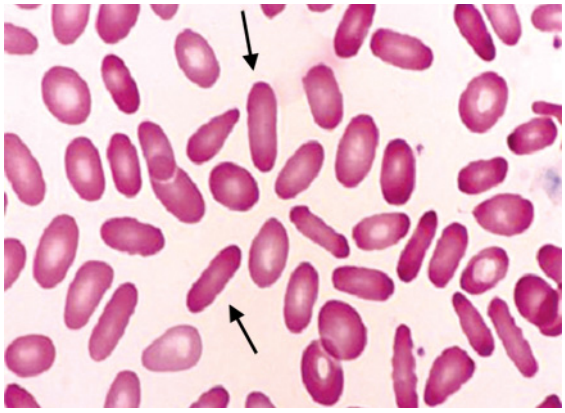


Fig. 23.14: Elliptocyte—note the oval shape (arrows)

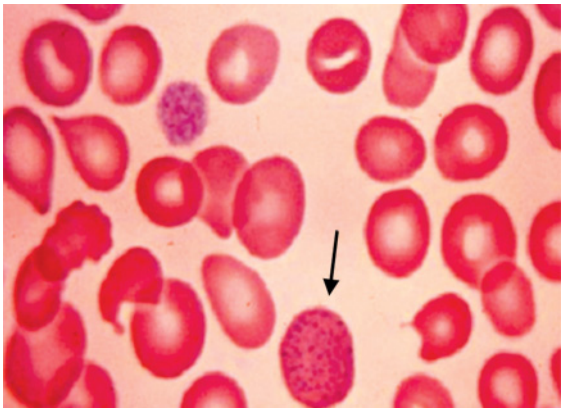


Fig. 23.12: Basophilic stipling—note the basophilic dots in the RBC, often due to toxic injury (arrow)

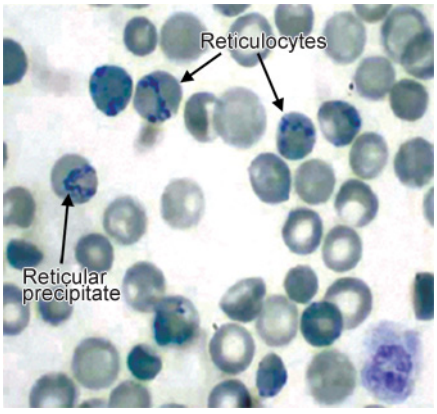


Fig. 23.15: Reticulocytes—note the reticulum in the substance of the RBC (arrows)

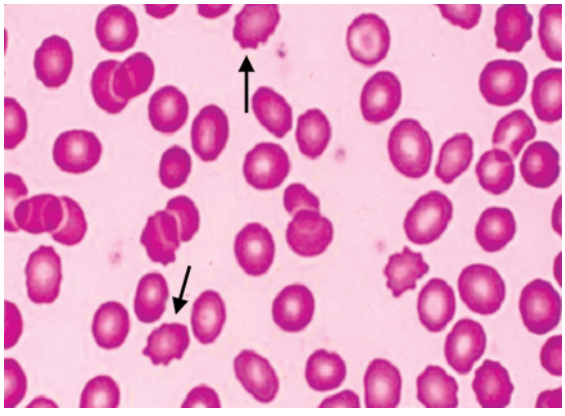


Fig. 23.13: Echinocytes—RBC with toothed margins (arrows)

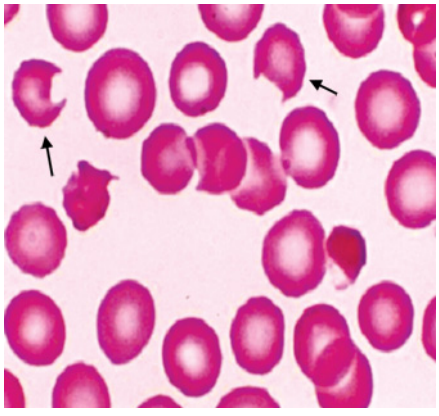


Fig. 23.16: Keratocyte; (syn horn cells), helmet cell or bite cell. Note the defect caused by loss of peripheral cytoplasm (arrows)

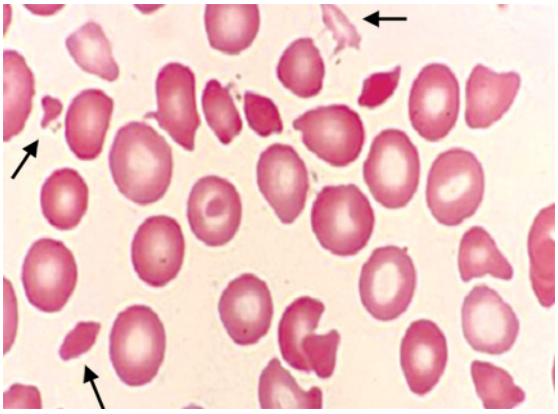


Fig. 23.17: Schistocyte—note the broken fragments of erythrocytes (arrows)

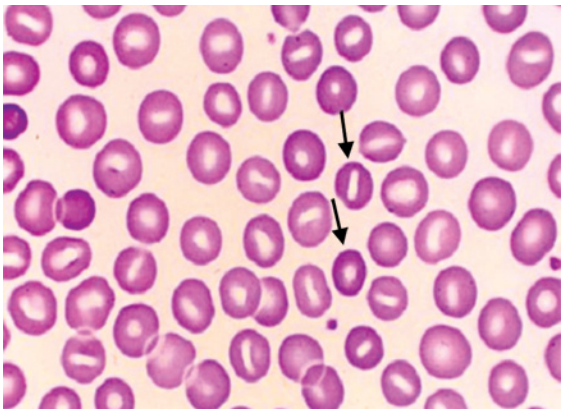


Fig. 23.20: Stomatocyte—mouth like cleft in the RBC (arrows)

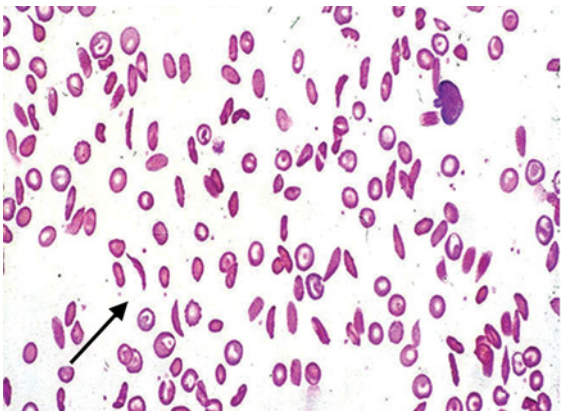


Fig. 23.18: Sickle cells—note the sickle shape due to the presence of HbS (arrow)

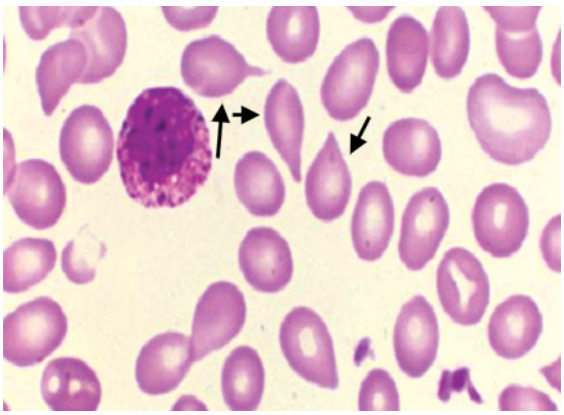


Fig. 23.21: Teardrop cells (arrows)

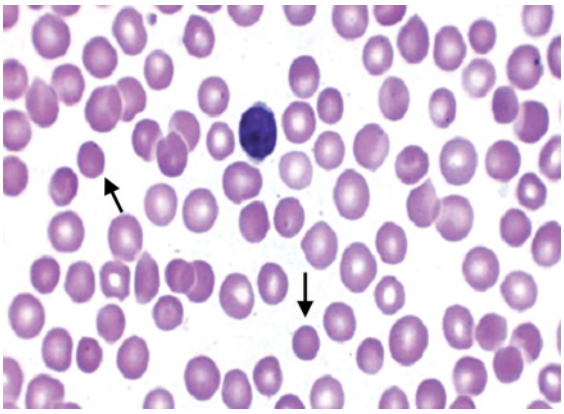


Fig. 23.19: Spherocytes—note smaller size and increased density of the erythrocytes which are convex (arrows)

Inclusions

Red cell inclusions seen are:

1. *Cabot's rings:* Ring like or figure of eight like structure the exact composition of which is not clear, probably nuclear, seen sometimes in megaloblastic anemia.
2. *Howell-Jolly bodies:* Small nuclear remnants spherically shaped and having the color of a pyknotic nucleus. In pathological situations they appear to represent separated chromosomes from the mitotic spindles during abnormal mitosis. They are characteristically present in the blood of splenectomized individuals and patients with asplenia, hemolytic anemia, and megaloblastic anemia. Red cell precursors such as reticulocytes (containing reticulum which is cytoplasmic in origin) and normoblasts are seen in hemolytic process.

Punctate basophilia is the presence of multiple dot-like basophilic bodies in the erythrocytes. These may be seen in lead poisoning and hemolytic anemia caused by toxic agents and several other conditions such as myelodysplastic syndromes and leukemias.

Occasionally erythroblasts may be seen in peripheral blood (normoblast or megaloblast) in conditions where there is an active regeneration. For example, after acute hemolysis or hemorrhage or even during treatment of nutritional anemias. In dyshematopoiesis distorted erythroblasts or their fragments may be seen in peripheral blood (Figs 23.2 to 23.21).

Malarial parasites should be looked for in all cases, irrespective of the presenting symptom.

Characteristics to identify malarial parasites are given below:

1. They are intraerythrocytic.
2. Cytoplasm is blue when stained by Romanowsky stains.
3. Chromatin is red.

Shape of the parasites, their number and size depend upon their species and the stage of their development.

Bartonellosis is a bacterial infection in which *Bartonella bacilliformis* is found within the RBCs. This infection is only rarely reported from India.

Other parasites seen in blood slides include trypanosomes, (not commonly found in India), Leishman-Donovan bodies are rarely seen in the macrophages in peripheral blood in leishmaniasis. They are seen more abundantly in the bone marrow and splenic puncture blood. Microfilaria (*Wuchereria bancrofti*, *Brugia malayi*) and others can be seen in endemic areas. In wet film the microfilaria are actively motile (Figs 23.22 to 23.25).

RETICULOCYTES

These are the early forms of RBC derived from erythroblasts. Reticulum is not demonstrable by the usual Romanowsky stains. A wet preparation is made by mixing one drop of blood (by finger prick) and one drop of a supravital stain (brilliant cresyl blue or methylene blue). After applying a coverslip this is kept for 2 to 3 minutes, and examined under oil immersion. An alternate method is to make a smear after mixing a drop of blood with the vital stain and counter-stain the slide with Leishman stain. Around 200 to 500 RBCs are examined for reticulocytes. Normal reticulocyte count is 0.8 to 1.5%. This is increased in hemolytic states and regenerating anemias. The count is reduced in aplastic anemia.

Since the reticulocyte count is expressed as a percentage of the erythrocytes, errors are likely to occur when erythrocyte counts and PCV vary. This error is obviated either by doing *absolute reticulocyte count* or using a correction factor. Correction for anemia:

$$\text{ARC} = \text{ORC} \times \frac{\text{HB}}{15} \text{ or } \text{ORC} \times \frac{\text{PCV}}{45}$$

Note: ARC—absolute reticulocyte count, ORC observed RC, PCV—packed cell volume.

Parasites in Peripheral Blood Film/Marrow (Figs 23.22 to 23.25)

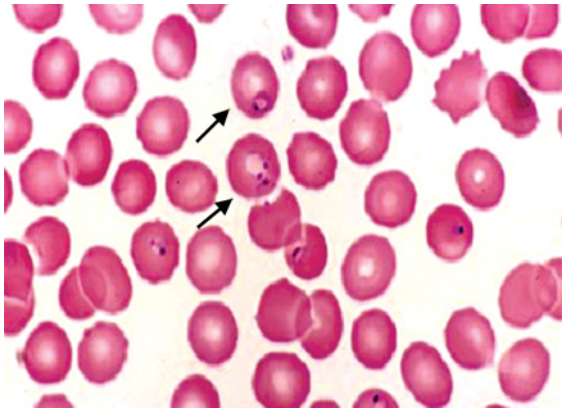


Fig. 23.22: Malarial parasites—*P. falciparum* (arrows)

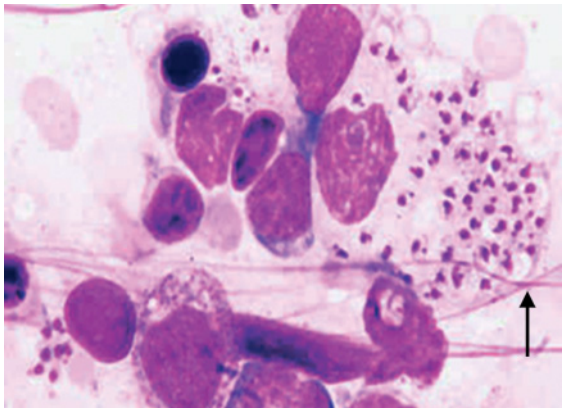


Fig. 23.23: LD bodies within macrophages in the marrow (arrow)



Fig. 23.24: Microfilaria *W. bancrofti*—note the smooth curves and the clear speces in front and back

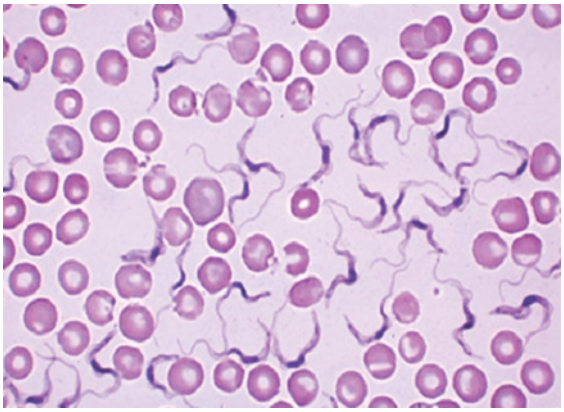


Fig. 23.25: Trypanosomes in peripheral blood—note the flagellum and undulating membrane

Abnormalities of Leukocytes and Plasma Cells in Leukemias and Myeloma (Figs 23.26 to 23.37)

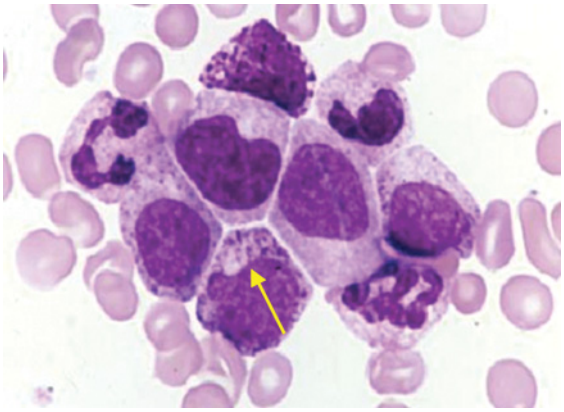


Fig. 23.26: Chronic myeloid leukemia. Peripheral blood—note myelocyte (arrow)

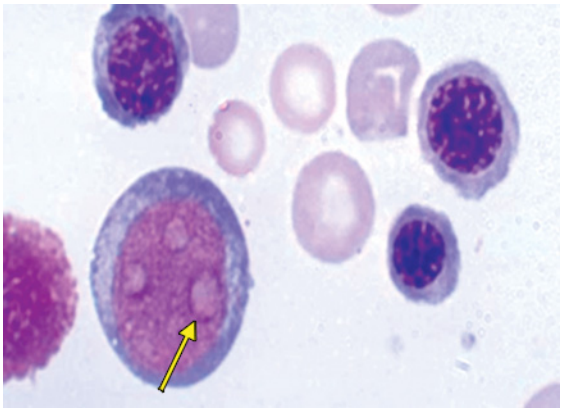


Fig. 23.27: Myeloblast in acute myeloid leukemia. Note the nucleoli in the blast (arrow)

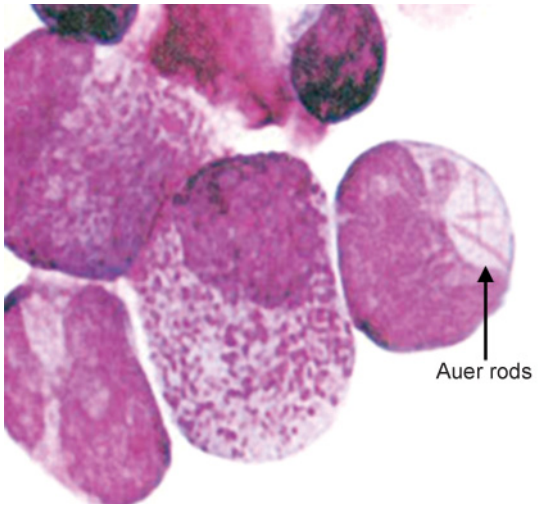


Fig. 23.28: Acute myeloid leukemia peripheral blood. Note Auer rods in the cytoplasm of the blast cell (arrow)

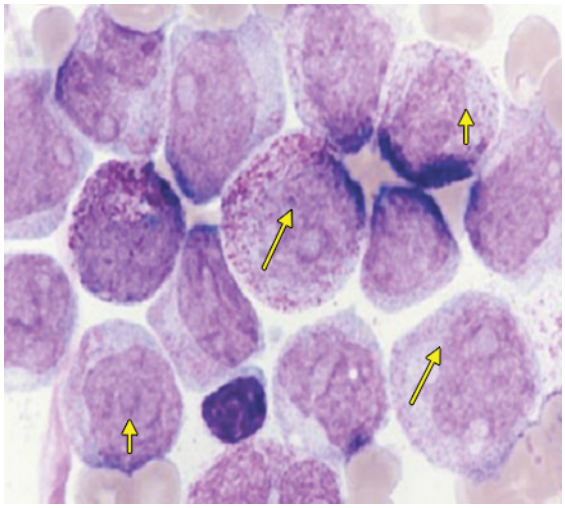


Fig. 23.29: Acute promyelocytic leukemia (M_3). Numerous blasts (arrows) and promyelocytes (arrowheads)

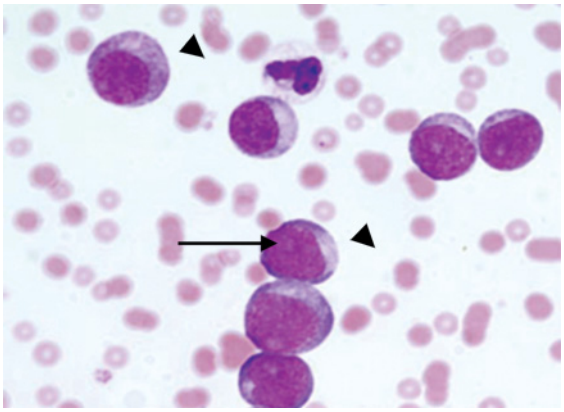


Fig. 23.30: Acute myeloid leukemia (M_1) numerous myeloblasts (arrow) and arrowheads point to Auer rods

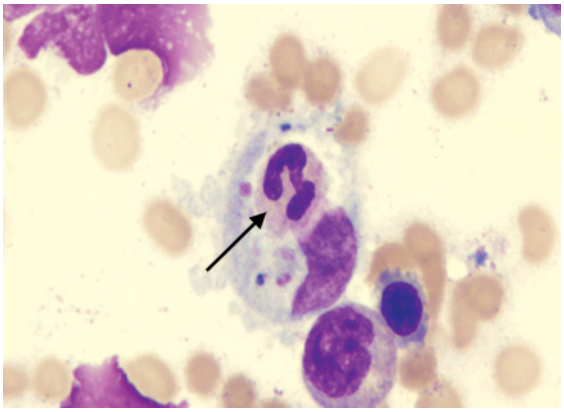


Fig. 23.33: Hemophagocytosis-of-neutrophil by macrophage. Note the engulfed neutrophil (arrow)

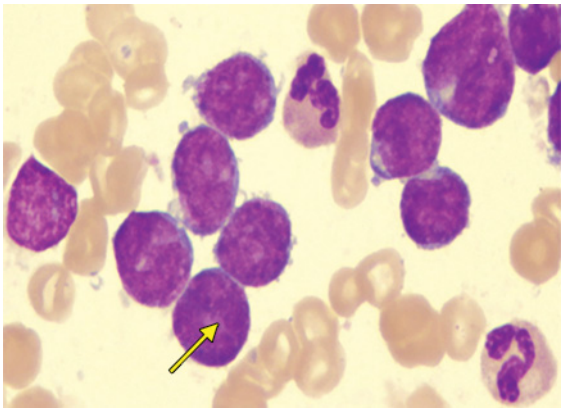


Fig. 23.31: Acute lymphatic leukemia. Note the nucleolus (arrow)

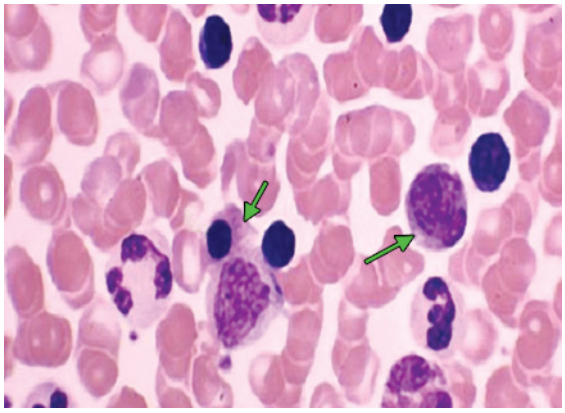


Fig. 23.34: Leukoerythroblastic blood picture. Note leukocyte precursors (arrow) and erythroid precursors (arrowhead) in peripheral blood

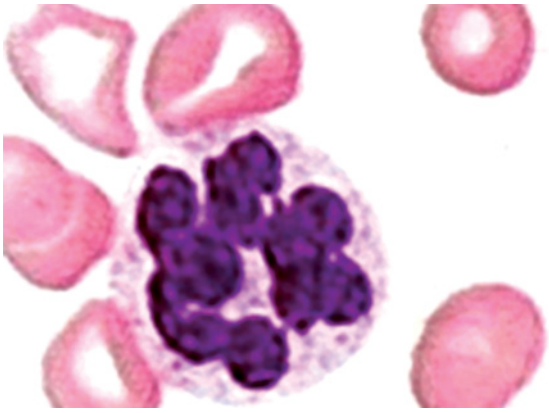


Fig. 23.32: Macropolycyte—note the excessive number of nuclear lobes in the neutrophils a finding in macrocytic anemia

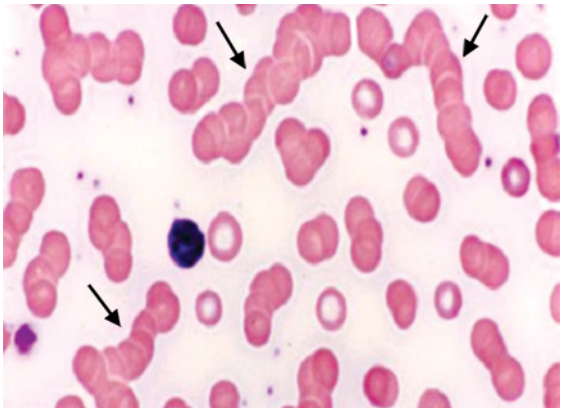


Fig. 23.35: Peripheral blood film showing rouleauxing (arrows) indicates high ESR

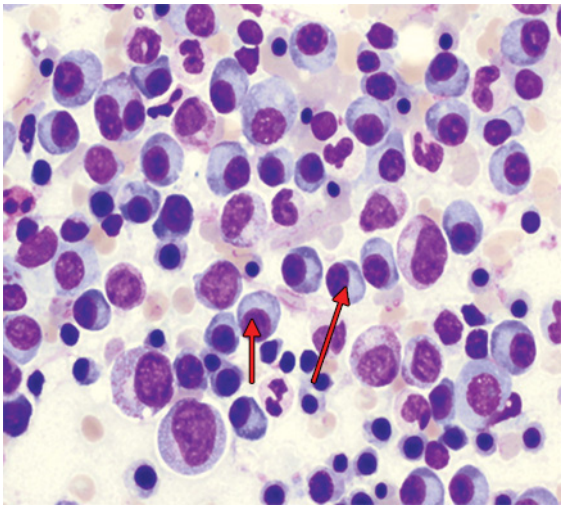


Fig. 23.36: Plasma cells, in bone marrow in multiple myeloma. *Note:* The plasma cells (arrows)

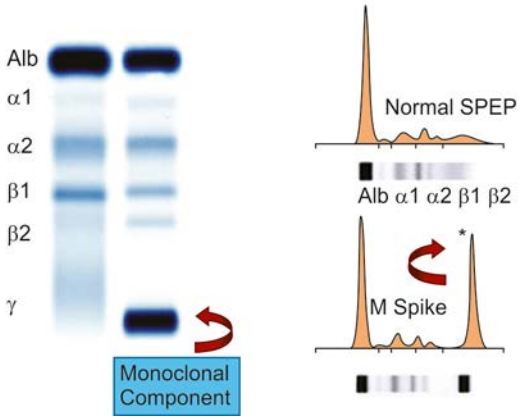


Fig. 23.37: Serum protein electrophoresis multiple myeloma. *Note:* The monoclonal M-band (asterisk)

Reticulocyte Production Index (RPI)

This is an index of erythrocyte regeneration. This is calculated from the corrected reticulocyte count, PCV and a constant the "shift factor." The shift factor has been determined for different hematocrit values:

PCV (hematocrit)	Shift factor
45%	1
35%	1.5
25%	2
18%	2.5

Correction for Prematurely Released Reticulocytes

$$\text{Reticulocyte production index (RPI)} = \frac{\text{Corrected reticulocyte count}}{\text{Shift factor}}$$

If the peripheral blood smear does not show frequent polychromatophil erythrocytes there is no need for this correction.

Calculation of RPI—example.

If a patient has a PCV of 22.5% and reticulocyte count of 30% his corrected reticulocyte count is: (where 45 is the normal PCV)

$$\frac{30 \times 25.5}{45\%} = 15$$

$$\text{RPI} = \frac{\text{Corrected-reticulocyte}}{\text{shift factor}} = \frac{15}{2} = 7.5$$

The shift factor indicates the premature shift of the reticulocytes from the bone marrow to the peripheral blood according to the severity of anemia.

Where the shift factor for a PCV of 25% is 2. If the RPI is 7.5%, it indicates, that erythrocyte production is increased to 7.5 times the normal rate

Packed cell volume (Syn—Hematocrit): Estimation of packed cell volume (PCV) or hematocrit is a standard hematological parameter which is very reliable, being reproducible and accurate. It is important to use the proper speed and timing of the centrifugation, i.e. 3000 rpm for 30 minutes. The original method of using standard hematocrit tubes has been modified by using microhematocrit tubes. Automated machines give the hematocrit values accurately.

Red cell indices: Mean corpuscular hemoglobin (MCH), mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) can be calculated from the hemoglobin, erythrocyte count and the PCV. Normal MCH is 27 to 32 pg. Normal MCV is 76 to 94 fL and it is increased in macrocytosis. Normal MCHC is 32 to 36 g/dL. Values below 27 g/dL suggest iron deficiency anemia.

ERYTHROCYTE SEDIMENTATION RATE

Normal erythrocyte sedimentation rate (ESR) is up to 10 mm/hour in men and 15 mm/hour in women. ESR is a nonspecific acute phase reactant and may be increased in several diseases. Among the hematological diseases, multiple myeloma, acute leukemia and hemolytic anemias give very high values. The ESR tends to increase nonspecifically whenever haemoglobin falls. ESR is characteristically low in polycythemia and congestive cardiac failure. When an unexpectedly low value is obtained, it should be checked whether the blood has clotted in the Westergren ESR tube.

LEUKOCYTES

They are concentrated at the tail end and the margins of the peripheral smear. Larger cells like granulocytes and monocytes move to the periphery whereas smaller cells like lymphocytes remain in the central portion of the film.

Differential leukocyte count should be done from the peripheral smear by counting 100 consecutive cells in a manner so that all representative areas of the slide are covered.

The normal differential count in adults is:

- Neutrophils 55-60%
- Lymphocytes 30-40%
- Eosinophils 1-5%
- Monocytes 2-8%
- Basophils 0-1 %

An occasional normoblast may be seen. Otherwise immature cells are not seen in the peripheral blood.

The number of lobes in the neutrophils indicates their age. Young polymorphs generally have only two lobes. Hypersegmented neutrophils with more than 5 lobes (macropolycytes) (Fig. 23.32) are found in megaloblastic anaemia. Toxic granulations occur in high fevers and infections.

Granulocytes are very susceptible to drug toxicity. Agranulocytosis is a dreaded complication caused by drugs such as phenylbutazone, chloramphenicol, antithyroid drugs and others. In the early stages the younger forms disappear. Later there may be almost total neutropenia. Since early withdrawal of the drug is life saving, it is advisable to do *an Arneth count* (counting the lobes in the nuclei) early in the disease if agranulocytosis is suspected. The normal distribution of neutrophils is given below:

- 1 lobe 5%
- 2 lobes 35%
- 3 lobes 41%
- 4 lobes 17%
- 5 lobes 2%

Immature cells in the peripheral smear should be carefully studied. Sometimes their number may be very small and they may be missed (Figs 23.22 to 23.36).

Buffy coat smear: The buffy coat which forms at the top of the RBC column while doing the hematocrit estimation in a PCV tube after centrifugation contains leukocytes and platelets almost entirely. When smeared on a slide and examined after staining with Leishman stain one may detect immature white cells, nucleated red cells and plasma cells which may contribute to a definite diagnosis. Inspection of the PCV tube gives a preliminary idea about the number of leukocytes and platelets.

PLATELETS

Platelets are seen as non-nucleated bodies which may occur in clumps or singly. Normal platelets undergo aggregation. If platelet count is normal, absence of clumping indicates thrombocytopathy. When the platelet count is less than 10,000/cmm, only an occasional platelet will be seen in an ordinary film. Platelets may vary in size. When they exceed 4μ—in diameter they are called *macrothrombocytes.* These are seen in immune thrombocytopenias. Normal mean platelet volume is 7.1 to 11.1 fL. Manual counting or even automated counters may not give accurate values when the platelet count is less than 20,000/cmm. It is therefore absolutely necessary that in such cases a peripheral blood smear should be examined to confirm the presence of severe thrombocytopenia. Megakaryocytic fragments may be seen occasionally in conditions like myelodsyplastic syndromes (MDS), rapid regeneration of anemias and megakaryocytic leukemias.

DIAGNOSIS OF LEUKEMIA

Blood Film Examination

Leukemia is a primary neoplastic process involving the leukocyte precursors in the bone marrow. This is characterized by leukocytosis and the presence of immature leukocytes in peripheral blood. In

subleukemic leukemias the total leukocyte count is not elevated but leukocyte precursors may be seen. In aleukemic leukemia the peripheral blood does not contain abnormal cells, but bone marrow reveals them.

Leukemoid reaction is the presence of immature leukocytes in the peripheral blood with moderate or severe leukocytosis, often secondary to other conditions.

Conditions giving rise to leukemoid reaction.

Myeloid reaction	Pneumonia, meningitis, diphtheria, amebic liver abscess tumors with metastasis to the bones
Lymphatic reaction	Disseminated tuberculosis, pertussis, infectious mononucleosis, infective hepatitis

It is possible to diagnose 50 to 70% of all leukemias by examining the peripheral smear (Tables 23.1 and 23.2). In more than 2/3 of all leukemias there may be leukocytosis. In the rest the count is normal or low (subleukemic leukemia).

General Points to Identify Leukemias

Leukocytes (Figs 23.26 to 23.34)

a. Gross or moderate increase in the number of a particular type of cell, e.g. granulocytes and myelocytes in chronic myeloid leukemia, mature lymphocytes in chronic lymphatic leukemia, myeloblasts in acute myeloid leukemia, lymphoblasts in acute lymphatic leukemia.
b. Presence of blast cells above 20% is suggestive of acute leukemia.
c. Suppression of the other normal leukocytes, e.g. neutropenia in acute leukemia (Table 23.1).

Erythrocytes: Generally there is a suppression of erythropoiesis and therefore various grades of anaemia develop, especially in acute leukemias.

Platelets: They are considerably reduced in acute leukemias especially so in those associated with bleeding. When the platelet count falls below 50,000/cmm spontaneous bleeding is common.

Classification of Acute Leukemias

Acute leukemias are further subclassified based on morphology and immunological features.

Acute myeloid leukemia (AML)—French, American, British (FAB) classification.

Subclass	*Type of cell*
M0	Minimally differentiated
M1	Undifferenciated myeloblast
M2	Myeloblasts typical
M3	Promyelocytic
M3V	Hypogranular variant
M4	Myelomonocytic

Table 23.1: Peripheral blood findings in acute leukemias, chronic leukemias, leukemoid reactions and myelodysplastic syndrome

Parameter	*Acute leukemias*	*Chronic myeloid leukemia*	*Chronic lymphatic leukemia*	*Leukemoid reaction*	*Myelodysplastic syndrome*
1. Total WBC	Moderately increased (20-30,000/ cmm or more)	Very high 100,000 cmm and above	Above 50,000/cmm	High and variable	Normal low or HIgh
2. Blast cells	>20%	Only a few	None	May be present but very few	Scanty or small numbers in some
3. Myelocytes	Present in small numbers except in acute promyelocytic leukemia	Found in large numbers	Nill	Predominant cell in myeloid reaction	Seen
4. Lymphocytes	Variable	Very few	Almost all cells adult lymphocytes	Predominant cell in lymphatic leukemoid reaction	Normal
5. Platelets	Reduced	Normal or increased	Normal or decreased	Normal or increased	Generally decreased
6. Nature of disease	Neoplasm	Neoplasm	Neoplasm	Secondary to other conditions, often nonneoplastic	Premalignant
7. Leukocyte alkaline phosphatase (LAP) score	Variable	Low	Not-applicable	Increased	Low/variable
8. Chromosomal change	Several changes	Ph chromosome diagnostic	Diagnostic changes present	Nil	Often present and diagnostic

Table 23.2: Lineage dependent leukemias-immunological markers of cell types

Lymphoid lineage		*Nonlymphocyte lineage*	
Cell type	Antigen	Myeloid cell	CD_{13},CD_{33},CD_{11b},CD_{15}
B-lymphocyte	CD_{19},$CD_{20}$$CD_{21}$, CD_{22}, CD_{23},CD_{24}	Monocytic cells	$CD_{14}$$CD_{1lb}$
Plasma cell	CD_{3S} Cytoplasmic immunoglobulin	Megakaryocyte	CD_{41},CD_{42b},CD_{61}

M4E	With eosinophilia
M5	Monocytic
M5a	Monoblasts 80%
M5b	Monoblasts 20%
M6	Erythroleukemia
M7	Megakaryoblastic leukemia

Acute Lymphatic Leukemia FAB Classification

When stained with Wright's stain three types—L1, L2 and L3 can be distinguished.

- *L1:* The blast cells are small and there is no appreciable variation in size and shape. The nuclear chromatin is smooth and the nucleoli are indistinct.
- *L2:* The blast cells vary in size with prominent nucleoli and a variable amount of cytoplasm.
- *L3:* The cells are deeply basophilic with vacuolated cytoplasm.

Immunological markers and other cytochemical markers help to determine the cell precisely. These tests are to be done in specialized laboratories.

The cluster of differentiation or cluster of designation (CD) antigens are cellular molecules that are recognized by monoclonal antibodies. The molecule's biochemical properties and cellular distribution are thus identified. The CD number for each molecule is defined at international workshops where such monoclonal antibodies are exchanged and their ability to react with human cells and or human cell molecules are compared. Now CD has become a protocol used for the identification and investigation of cell surface molecules present on the white blood cells. The CD molecules act in different ways. Some act as receptors or ligands initiating cell signaling. Some have other functions as cell adhesion. CD for humans is numbered upto 350 most recently. CD is found out by flow cytometry (Table 23.2).

Surface antigens that are not lineage dependent

1. HLA-DR, HLA Class II
2. Leukocyte common antigen—CD_{45}
3. Stem cell antigen—CD_{34}
4. Common acute lymphatic leukemia antigen (CALLA)–CD_{10}

When the number of leukocytes in the peripheral smear is sparse the *buffy coat* obtained from a hematocrit tube may be examined to get a concentration of cells. This helps to identify abnormalities if any.

BONE MARROW EXAMINATION

This is one of the confirmatory investigations in most of the hematological disorders. Bone marrow may be obtained by the following procedures (Figs 23.38 and 23.39).

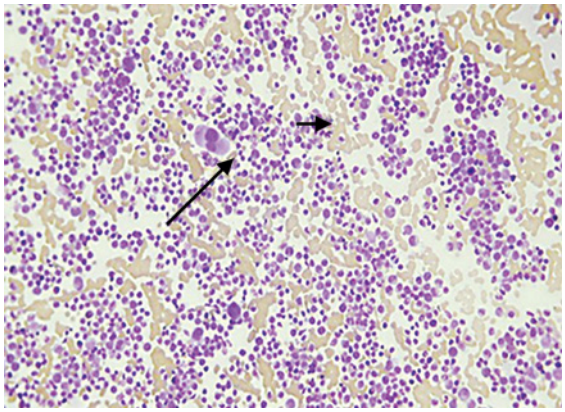


Fig. 23.38: Normal bone marrow—note the cellularity (arrow) and the stroma (arrowhead) low power view

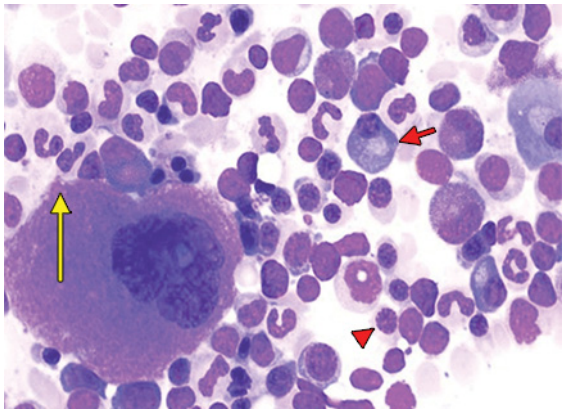


Fig. 23.39: Normal bone marrow × 1000 (Megakaryocyte)—note the large cell with irregular margins (arrow shows escaping platelets). Normoblast (short arrow). Plasma cell (arrowhead)

1. Aspiration.
2. Trephine biopsy.
3. Open biopsy.

Indications for Bone Marrow Aspiration

Conditions where bone marrow examination is confirmatory:

1. Hypoplasia of the bone marrow.
2. All leukemias.
3. Megaloblastic anemia.
4. Multiple myeloma.
5. Myelodysplastic syndrome (MDS).
6. Immune thrombocytopenia and secondary thrombocytopenia.
7. Waldenstrom's macroglobulinemia.
8. Sideroblastic anemia.
9. Storage diseases like Gaucher's disease.

Conditions in which a bone marrow study is very helpful:

1. Unexplained anemias.
2. Parasitic infections like leishmaniasis and malaria.
3. Investigation of pyrexia of unknown origin especially in infection by *Salmonella typhi*.
4. Karyotyping in hematological disorders, e.g. Ph' chromosome in chronic myeloid leukemia and nonhematological conditions such as Turner's syndrome and Klinefelter's syndrome.
5. Secondary malignant deposits in the bone marrow.
6. To demonstrate iron stores and iron deficiency.
7. Staging lymphomas.

Therapeutic Indications

1. To collect bone marrow for transplantation from the donor.
2. For infusion of fluids under exceptional circumstances in children-site: Tibial marrow cavity.

Procedure: Following sites may be employed:

1. Iliac crest—posterior superior iliac spine being the commonest site. An alternate site is the anterior iliac spine.
2. Manubrium or the first piece of sternum.
3. Tibial shaft.
4. Occasionally the ribs and vertebral spine, especially when pathological lesions are detected in them.

Aspiration is done using a bone marrow aspiration needle *(Cox needle)* under local anesthesia. The material may be smeared on slides and stained for morphological studies or processed further for karyotyping microbiological culture, and others. In conditions like lymphoma some cases of acute leukemia, hairy cell leukemia bone marrow secondaries and other very hyperplastic conditions when marrow material is too thick and adherent to be aspirated, trephine biopsy is necessary. Trephine biopsy is also indicated in aplastic anemias and myelofibrosis when bone marrow cellularity is low and aspiration yields a "dry tap". Trephine biopsy is done by *Jamshidi's needle*. Disposable trephines are available. Imprint smears made from the specimen can be used for routine morphology and the core of the tissue is processed for histopathology. It is to be remembered that in many cases a dry tap is due to a faulty technique. At present, it is a common practice to take biopsy specimen also along with aspiration since histology gives additional information about the cellular and stromal elements.

SPECIAL INVESTIGATIONS IN NUTRITIONAL ANEMIAS

Iron Deficiency Anemia

Serum iron levels are decreased. Total iron binding capacity (TIBC) is increased. Normal serum iron levels range from 60 to 160 mcg/dL (13–32 P mol/L). Normal iron binding capacity (transferrin level) ranges from 280 to 400 mcg/dL (45–70 P mol/L). Normal transferrin saturation is 30 to 35%. Lower values less than 16% indicate iron deficiency.

Demonstration of iron stores in the bone marrow by "Prussian blue staining" is a reliable method to assess the iron status of the individual. The serum ferritin level is a very reliable indicator of the iron stores in the body. Normal values range from 15 to 200 ng/mL in males (mean 50.4) and from 12 to 125 ng/mL in females (mean 24). In conditions of iron overload such as thalassemia and hemochromatosis the values are very high.

Values of serum iron below 80mcg/dL is suggestive of iron deficiency. Transferrin saturation below 16% and low ferritin < 15 ng/mL in males and<12ng/mL in females) are very reliable indicators of iron deficiency except under special situations such as renal failure patients receiving hemodialysis.

Serum ferritin, being an acute reactant, is deceptively high in patients undergoing dialysis procedures.

Serum transferrin receptor (sTFR) estimation is a newer investigatory tool for iron deficiency. It is increased in iron deficiency and this distinguishes iron deficiency anemia from anemia of chronic diseases (ACD).

Macrocytic Anemias

Serum folate, red cell folate and serum vitamin B_{12}: Estimation of serum folate, red cell folate and serum, B_{12} reveals the causative factor in megaloblastic anemias.

Normal levels of vit B_{12}	140-980 ng/L
Serum folate	6-20 mcg/L
Red cell folate	160-640 mcg/L

Serum folate levels below 3 ng/mL and red cell folate levels below 100 ng/mL indicate folate deficiency. Serum vitamin B_{12} level below 100 ng/mL indicates deficiency of this vitamin.

DIAGNOSIS OF HEMOLYTIC ANEMIAS

General features to suggest hemolytic anemia:

A. *Signs of excess destruction of the RBCs:*
 1. Different grades of anemia.
 2. Presence of schistocytes in peripheral blood (Fig. 23.17).
 3. Increased levels of unconjugated bilirubin.
 4. Excess urobilinogen in the urine and high colored stools due to excess of stercobilin.
 5. Haptoglobins: These are proteins present in plasma which bind free hemoglobin. In hemolytic anemia levels of serum haptoglobins are reduced.

B. *Signs of compensatory erythropoiesis:*
 1. Increased reticulocyte count (Fig. 23.15).
 2. Presence of erythroid precursors (often normoblasts)—in the peripheral smear (Fig. 23.7).
 3. Excess of young forms of erythrocytes containing inclusions such as Cabot's rings and Howel Jolly bodies (Figs 23.8 and 23.9).
 4. Widening of marrow spaces demonstrable by X-ray of skull, hair on end appearance phalanges, etc.
 5. Studies of red cell life span using isotopes. The site of RBC destruction and the life span of RBCs are determined by isotopic studies using radioactive chromium.

Immunological Studies

After establishing the presence of an active hemolytic process further investigations are carried out to determine the specific cause.

Characterization of Antibodies

Antibodies may be complete (usually IgM) or incomplete (usually IgG). The complete antibodies are capable of agglutinating suspended erythrocytes whereas incomplete antibodies require the presence of other reagents like *antiglobulin serum (Coombs' serum).* Warm antibodies are active at body temperature (37°C). Cold antibodies are demonstrated by performing the test at 4° C.

Determination of the major blood groups A, B, O and Rh, and minor blood groups in special cases help to bring out blood group incompatibility and transfusion related hemolytic anemias.

Antiglobulin Test (Coombs' Test)

This test detects the presence of incomplete antibodies and provides evidence of immune hemolysis. Direct Coombs' test detects the presence of antibodies on the surface of erythrocytes, and indirect Coombs' test detects them in the serum.

Estimation of Red Cell Enzymes

Glucose-6-phosphate dehydrogenase (G6PD) is deficient in many ethnic groups in India. Low levels of this enzyme predispose to drug induced and spontaneous hemolysis. Other enzymes can also be estimated. Young erythrocytes are generally rich in G6PD and, therefore, when there is marked reticulocytosis following acute hemolysis the enzyme level may be normal even in affected individuals.

Heinz Bodies

These are inclusions which develop in RBCs in the presence of hemolytic anemia caused by toxic agents. They can be demonstrated when blood is incubated *in vitro* with the suspected material. Heinz bodies are also seen in the presence of unstable hemoglobins such as Hb K and Hb H. Demonstration of Heinz bodies may give clue to the cause of hemolysis.

Determination of Osmotic Fragility

Normal RBCs lyse in saline of strength between 0.45% and 0.3%. Increase in osmotic fragility is very suggestive of hereditary spherocytosis. In thalassemias osmotic fragility is decreased.

Estimation of Fetal Hemoglobin and Abnormal Hemoglobins

Fetal hemoglobin is estimated by the alkali denaturation test, using the patients' hemoglobin. Fetal hemoglobin is more resistant to alkali denaturation. Levels above 4% of fetal hemoglobin occur in thalassemias, thalassemic syndromes and less commonly in long standing acquired or congenital anemias.

Abnormal hemoglobins such as HbS, HbE and others can be estimated by electrophoresis. Presence of HbS can be demonstrated by the sickling test. A drop of fresh blood is incubated with a drop of 2% solution of sodium metabisulphite and examined under the microscope for sickling. Presence of sickling suggests the presence of HbS.

Paroxysmal nocturnal hemoglobinuria is a rare disorder. This is diagnosed by **sucrose lysis test** *and* **acidified—serum test (Ham test***)*. Newer tests include the analysis of molecules on the surface of hematopoetic cells by flow cytometry. Absence of CD55 and CD59 and other antigens is diagnostic.

Cytogenetic analysis in hematology: Demonstration of the karyotype to study the chromosomal abnormalities helps to characterize and prognosticate several genetically determined diseases such as mongolism and Fanconi's anemia and acquired diseases such as leukemias and myelodysplastic syndrome (Tables 23.3 to 23.5).

At present cytogenetic analysis has reached a high level of perfection and the complete diagnosis and evidence based management of many hematological diseases should include the cytogenetic pattern as well.

Genetic analysis and molecular biological methods such as demonstration of the presence of abnormal genes and their products help to make exact diagnosis in hemoglobinopathies thalassemias and others. Prenatal diagnosis obtained by analysis of material obtained by amniocentesis or chorionic villous biopsy helps to arrive at treatment decisions such as termination of the affected pregnancy.

Flow cytometry is used for identification of cell markers in hematology. It works on the principle of light scatter. When cells move in a fluid column and interrupt a beam of laser light, light scatter occurs. The subpopulations of hemopoetic cells can be recognized by analysis of the light scatter. Identification of cell populations and cell surface markers is achieved with monoclonal antibodies tagged with florescent dyes. These antibodies are specific for the cell surface markers. Flow cytometry is widely used in hematology laboratories to assess cell differentiation and to detect maturation-related cellular proteins. DNA content can be estimated using DNA-binding dyes.

Uses of flow cytometry—classification and diagnosis of:

1. Acute leukemia and lymphomas.
2. Assessment of granulocyte function.
3. Platelet function.
4. Diagnosis of paroxysmal nocturnal hemoglobinuria (PNH).

Fluorescence in situ hybridization (FISH) is a new molecular cytogenetic technique that has wide applications in hematology-oncology. It is a rapid and reliable diagnostic test that is currently available in only a few centers in India. The FISH makes use of molecular probes marked with a fluorescent dye that corresponds to a gene or DNA sequence and shows a bright signal under the fluorescence microscope at a specific locus on a chromosome. Differently colored probes for various chromosomes, or different loci on the same chromosome can be used. The FISH technique is also known as "interphase cytogenetics" and it has revolutionized in the field of clinical genetics. FISH can be done directly and is mainly an overnight procedure. Hence, the report can be available the next day itself. The FISH technique supplements conventional cytogenetics and in some cases, provides additional information, which is not detected by karyotyping.

LEUKEMIAS—CYTOGENETIC INVESTIGATIONS

Many haematopoietic malignancies are characterized by specific chromosomal abnormalities. Identification of these help in specific diagnosis, management, prognosis and confirmation of cure in such cases.

Cytogenetic analysis provides a most useful tool for the identification of genotypical changes Chromosomal changes that affect regions greater than approximately 3000 to 5000 kb only can be detected.

Cytogenetic studies can be useful firstly for monitoring the response to therapy and secondly for detecting relapse and distinguishing relapse from a new therapy—related leukemia or lymphoma during follow-up (Tables 23.3 to 23.5).

Table 23.3: Cytogenetic abnormalities that confirm the diagnosis

Cytogenetic abnormality	*Diagnosis*
• (9;22) (q34;q11)	Chronic granulocytic leukemia
• (5;12) (q33; p13)	Chronic myelomonocytic leukemia with eosinophilia with PDGFb-TEL fusion
• (8;21) (q22;q22)	M2 AML with AMLl-ETO fusion
• (15;17) (q22;q12-21)	M3 or M3 variant AML with PML-RARa fusion.
• (14;18) (q32;q21), t(2;18)	Follicular lymphoma or large cell
• (P12;q21) or t(18;22)	transformation of follicular lymphoma
• (q21;q11)	
• (8;14)(q24;q32), t(2;8)	Burkitt's lymphoma or L3 subtype of ALL
• (p12;q24) or t(8;22) (q24;q11)	
• (2;5) (P23;q35)	Anaplastic large cell lymphoma

Table 23.4: Chromosomal abnormalities in some varieties of lymphatic leukemia

Rearrangement	*Typical morphology*	*Typical immunophenotype*
del/t (12p)	L_1, L_2	Common ALL
del (6q)	L_1 ,L_2	Common ALL
t(8;14) (q24;q11)	L_1, L_2	T-ALL
t(8;14)(q24;q32)	L_3	B-ALL
t(8;22)(q24;q11)	L_3	B-ALL
t(2;8) (p12;q24)	L_3	B-ALL
t(l;11) (p32;q23)	L_1	Pre-B ALL
t(1;19)(q23;p13)	L_1	Pre-B ALL

Note: The morphological features overlap for different types of acute lymphatic leukemia.

Table 23.5: Specific chromosome changes in lymphomas and chronic lymphatic leukemia

t(2;8)(p12;q24)	Burkitt's lymphoma
t(3;22) (q28;q11)	Diffuse large B-cell lymphoma
t(14;19)(q32.3;q13.1)	Chronic lymphocytic leukemia
t(11;14) (q13;q32)	Chronic lymphocytic leukemia and diffuse small cell lymphoma

Real-Time PCR (RT-PCR)

Molecular biological techniques have offered us a radical improvement in the evaluation of hematological disorders. Aberrant fusion transcripts of chromosomes (CML, AML, ALL), e.g. Bcr-Abl of Ph chromosome can be accurately estimated. RT-PCR can be done during diagnosis, treatment and follow-up especially to know about minimal residual disease (MRD). One leukemic cell in roughly 1000,000 normal cells can still be identified. Fusion genes in lymphoma, rearranged immunoglobulins and others can be estimated by RT-PCR.

The main indications for cytogenetic investigations are:

At diagnosis:

a. To confirm the diagnosis.
b. To predict the prognosis and plan therapy.

During follow-up:

a. To confirm regression and cure and to detect relapse early.
b. To confirm engraftment after bone marrow or stem cell transplant.

Cytogenetic analysis helps to distinguish between benign and malignant conditions which may resemble each other morphologically, e.g. hypereosinophilic syndrome from eosinophilic leukemia, myelodysplastic syndrome from aplastic anemia, neutrophileukocytosis from chronic myeloid leukemia and others. Several cytogenetic abnormalities have been identified.

Microarray

Microarrays are fast becoming routine tools for analysis of gene expression (which is specific for a patient) in a number of hematological disorders. This will have and immense impact on the classification, treatment and prognosis of many hematological disorders.

BLEEDING DISORDERS

Tests for Coagulation Abnormalities

Among the generalized bleeding tendencies, two thirds are due to platelet-capillary abnormalities (purpuras). The remaining third are due to abnormalities of coagulation mechanism or abnormal fibrinolysis.

Preliminary Investigations in a Patient with Generalized Bleeding Disorder

Bleeding Time

This is done by noting the time taken for spontaneous arrest of bleeding from a cut in the capillary system. Bleeding time depends upon the adequacy of platelet number and function, and capillary integrity. This test is standardized (Ivy) by using a template for incision over the forearm and applying a pressure of 40 mm of mercury proximally using a sphygmomanometer cuff. Normal bleeding time is up to 7 minutes. Above 10 minutes is abnormal.

Coagulation Time (Syn: Clotting Time)

Principle: The time taken for spontaneous clotting of freshly drawn blood at room temperature is noted. In theory, deficiency of any of the factors in the intrinsic and extrinsic pathways of coagulation should prolong the clotting time but in practice mild or even moderate deficiencies of several factors do not. Normal clotting time is 5 to 10 minutes. Clotting time is prolonged only if the defect is moderate or severe. In practice prolongation of the coagulation time is almost always caused by hemophilia, Christmas disease, disseminated intravascular coagulation, heparin therapy, fibrinogen deficiency or circulating anticoagulants.

Hess' Test (Capillary Fragility Test)

The fragility of the capillaries when submitted to higher pressure is revealed by the appearance of purpura distal to compression of the arm by a sphygmomanometer cuff inflated to 90 mm Hg and kept for five minutes. Platelet and vascular defects and several other conditions give rise to a positive test. Being nonspecific, this test is not of great diagnostic importance in hematology.

This test is important in determining the possibility of hemorrhagic complication in dengue hemorrhagic fever.

Clot Retraction

The tube in which the blood is allowed to clot is observed after one hour and two hours at 37°C. In normals the clot retracts and the serum exudes. This function depends on platelet activity. The process can be quantitated by measuring the volume of serum exuded. In platelet dysfunction and in thrombocytopenia clot retraction is defective. Normally the separated serum measures around 50%. Clot retraction is defective when the platelet counts fall below 50,000/cumm and in thrombocytopathies.

Fibrinolysis

The tube containing the clot is observed at regular intervals for 24 hours. Early lysis of the clot (within 2 hours) should suggest the possibility of excessive fibrinolysis.

Other Tests

Presence of excessive fibrinolytic activity of the plasma used to be demonstrated by *euglobulin lysis* time and lysis of fibrin plates. At present D-dimer estimation is preferred.

Prothrombin Time

This test denotes the integrity of the extrinsic and common coagulation pathway. It is a test commonly employed to monitor anticoagulant therapy with coumarin drugs. This is probably the most frequently done test of coagulation function, since many patients are at present on long-term anticoagulant therapy. The time taken for extrinsic thromboplastin (usually extracts of brain) to form a clot in recalcified platelet poor plasma at 37°C is noted. In the normal it ranges from 12 to 15 seconds and this is the prothrombin time (PT). The patient's PT is compared with that of a normal control (often pooled) plasma of normal persons done simultaneously under the same conditions. PT can be expressed as the absolute times obtained or as a ratio of the patient's PT with the PT of the control subjects.

Previously different laboratories used to employ different thromboplastins with varying potency and therefore the values showed great variation between different laboratories.

In order to standardize the test and avoid inter-laboratory variations, internationally standardized thromboplastin is used and the results are expressed as *international normalized ratio (INR)*. INR ranging from 1.5 to 3 are maintained to provide anticoagulation for different thromboembolic conditions.

Partial thromboplastin time (PTT) also known as activated partial thromboplastin time (APTT) measures the time required for the formation of thrombin and fibrin clot by the intrinsic coagulation pathway. When one or more of the coagulation factors, except factor VII, are reduced to levels below 30% of normal, the APTT is prolonged (normal value of APTT for most of the laboratories is 35 seconds). The missing coagulation factor can be identified and quantitated by repeating the test with the addition of plasma having known defects and noting the correction of APTT (modified APTT tests).

The conditions in which prothrombin time (PT) and partial thromboplastin time (PTT) are prolonged are listed below.

PT Prolonged

1. Deficiency of factor VII.
2. Deficiency of vit K, anticoagulant therapy with coumadin drugs and phenindione.

PTT Prolonged

No *clinical bleeding:* Deficiency of factors V, XII, high molecular weight kininogen, (HMWK), prekallikrein (PK),

Mild or rare bleeding - XI . *Frequent severe bleeding* - VIII- or IX.

Both PT and PTT Prolonged

Deficiency of factors II, V and X and vit K deficiency, anticoagulant therapy, circulating anti-coagulants. All these deficiencies can be corrected by substitution with normal plasma. In the presence of circulating anticoagulants (factor inhibitors) the tests will not be corrected by the addition of normal plasma.

Fibrinogen levels and detection of excessive fibrinolysis: The test used to detect fibrinolysis is euglobulin lysis time. This is shortened in hyperfibrinolytic states. Estimation of fibrinogen helps to detect the level of fibrinogen in blood and diagnose hyper- and hypofibrinogenemia. Presence of excess of *fibrin degradation products* (FDP) in serum and urine is diagnostic of accelerated fibrinolysis.

Thrombin time is prolonged when there is fibrinogenopenia, abnormalities of fibrin or presence of heparin and other circulating anticoagulants. When coagulation defects are caused by the deficiency of normal factors the abnormality can be corrected by the addition of 10 to 20% of normal plasma. In the presence of circulating anticoagulants normal plasma fails to correct the deficiency.

Rusven (Russel's viper venom) clotting time is employed to assay factor X and also for the detection of lupus anticoagulant.

At present quantitative and qualitative estimations of coagulation factors are undertaken in several advanced laboratories. These help to diagnosis subclinical deficiencies, inheritance pattern in relatives, detection of hereditary and acquired hyper coagulation states such as protein C and protein S deficiencies and qualitative abnormality of prothrombin.

TESTS FOR PLATELET FUNCTIONS

Since platelets play important roles in several disorders—both hematological and others (e.g. venous and arterial thromboemolism, ischemic heart disease, tissue repair, revascularization and others) testing platelet function has assumed importance. Broadly the tests may be grouped as follows:

1. Enumeration of platelets by automatic counters.
2. Studying the morphology.
3. Testing the functional capacity.
4. Identifying molecular defects in them.

Platelet counts: Normal platelet count is around 200,000/cmm (range 2-4 lacs/cmm). When platelet counts fall below *100,000*/cmm bleeding tendencies from mucous membrane and/or skin can manifest. The severity of bleeding and reduction in platelet count do not correlate in many cases.

Platelet count	*Tendency to bleed*
• <100,000/cmm	Bleeds on moderate trauma
• <50,000/cmm	Minimal trauma or even spontaneously
• <20,000/cmm	More marked spontaneous bleed.
• <10,000/cmm	Marked spontaneous bleed, mild coagulation defect may also occur

Morphology of platelets: Normal platelets are about 2 to 3 fL in volume. By microscopy platelets size can be assessed. A properly stained blood film should be examined. Platelet morphology cannot be properly studied if the blood film is under stained.

Large platelets (megathrombocytes) with platelet diameter more than 4μ occur in immune thrombocytopenias, regeneration of platelets and in thrombocytopathies like Bernard Soulier syndrome. Small platelets occur in thrombocytosis. The platelet size may vary. This can be shown by automatic cell counters. Further examination is by electron microscopy by which the granule content and cellular ultrastructure can be studied.

Tests for Qualitative Function of Platelets Aggregation

Platelet aggregometry is ideally done by aggregometer and thromboelastograph (which are automated instruments) or by manual methods. Aggregation in response to adenosine diphosphate (ADP), collagen, epinephrine, thrombin, arachidonic acid, ristocetin, and other substances can be studied.

Immunological Studies

Analysis of the surface glycoproteins: This is done by using monoclonal antibodies and flow cytometry. The platelet granules can be identified and quantitated by immunoassay.

Platelet mediated coagulation function: Estimation of fibrinogen, platelet factor III and IV release, von Willebrand is factor and others can be done by appropriate tests.

DISSEMINATED INTRAVASCULAR COAGULATION

In disseminated intravascular coagulation (DIC) since there is excessive consumption of coagulation factors and platelets, the clotting time and partial thromboplastin time (PTT) are both prolonged in addition to thrombocytopenia. The fibrinogen level is decreased. Fibrin degradation products (FDPs) are increased in serum and urine due to excessive secondary fibrinolysis.

In primary fibrinolysis PTT and the platelet counts are normal, but euglobulin lysis time is shortened and FDP levels are increased.

D-dimer Estimation

Plasma levels of fibrin D-dimer which is a degradation product of cross-linked fibrin indicate the rate of fibrinolysis. These assays are now freely available in many laboratories in India. D-dimer can be estimated by ELISA, latex agglutination or by whole blood agglutination.

D-dimer is one of the fibrin related markers (FRM). Plasmin cleaves both fibrin and fibrinogen at the same site. But when plasmin acts on covalently cross linked fibrin, D-dimers are released. Thus, D-dimers can be measured in the plasma as a relatively specific test of fibrin (rather than fibrinogen). It indirectly shows prior thrombin and fibrin clot formation and subsequent degradation by plasmin. D-dimer can be estimated by a variety of methods: semiquantitative vs quantitative, manual vs automated, latex agglutination vs ELISA. The normal value is 0.22 to 0.74 mcg/mL.

Clinical Significance

The D-dimer test provides a measure of fibrinolytic activity in the blood. Abnormal levels are found in bleeding and postoperative patients and in patients with deep venous thrombosis (DVT), disseminated intravascular coagulation (DIC), arterial thromboembolism (AT), pulmonary embolism (PE) and others. In addition, it has also been useful in the monitoring of thrombolytic therapy, cancer therapy and complicated myocardial infarction. Estimation of D-dimer is more specific than FDP in the diagnosis of disseminated intravascular coagulation

Non-specific increase in D-dimer occurs in old age, infections, inflammatory states, cancer, postoperative state, pregnancy and others.

INVESTIGATIONS IN THROMBOPHILIA

Thrombophilia is defined as an increased tendency to thrombosis after excluding acquired predisposing causes like trauma, immobility, DIC, pregnancy and others.

Inherited hypercoagulable states may be secondary to deficiency of inhibitors of natural clotting factors or elevated procoagulants or increased antagonists of fibrinolysis.

Hyperhomocysteinemia with homocystein levels greater than 18.5 mmol/L increases the thrombotic risk 2.5 fold.

Causes to thrombophilia are dipicted in Table 23.6

Table 23.6: Causes of thrombophilia

• The inherited hypercoagulable states
• Antithrombin III deficiency
• Protein C and S deficiency
• Disorders of the fibrinolytic system
• Disfibrinogenemia
• Factor V Leiden defect
• P 20210 (prothrombin abnormality)
• Hyperhomocysteinemia
• Increased in factors VIII, IX, XI levels
• Acquired causes – hyperhomocysteinemia – thrombocytosis – hyperviscosity states – antiphospholipid antibody syndrome

Screening Laboratory Tests

Prothrombin time (PT), activated partial thromboplastin time (APTT), and thrombin time (TT), the global tests of coagulation can be effectively used to guide further investigations.

In 20210 G mutation of prothrombin the prothrombin levels go above 115 IU/dL and this increases the risk of deep venous thrombosis.

APTT is shortened when coagulation factors II, VIII and XI are increased. Elevation of factor II should suggest P20210 mutation. Determination of the levels of antithrombin III (AT III), protein C, protein S and plasminogen activator inhibitor (PAI) help to diagnose their variations. ELISA and chromogenic tests are available to estimate AT III, protein C and protein S. Factor V Leyden is detected by molecular assays using PCR. Homocysteine levels are estimated by high performance liquid chromatography (HPLC) or ELISA. **Antiphospholipid antibody** is demonstrated by a combination of coagulation tests and immunological tests. Among the coagulation tests, APTT, Russel viper venom clotting time and kaolin clotting time are employed.

Immunological tests are used to detect antibodies against cardiolipin and other phospholipids such as phophatidyl serine.

Diagnosis of Multiple Myeloma

Generally myeloma presents with progressive anemia and bone pains. The vast majority are persons above the age of 55. ESR is often above 100 mm/hr. Examination of the buffy coat may show plasma cells which are characterized by deep blue cytoplasm, eccentric nucleus.

Generally myeloma presents with progressive anaemia and bone pains. The vast majority are persons above the age of 55. ESR is often above 100 mm/hr. Examination of the buffy coat may show plasma cells which are characterised by deep blue cytoplasm, eccentric nucleous and perinuclear halo. Diagnosis is confirmed if two or more of the following criteria are fulfilled (See Figs 23.36 and 23.37)

1. Bone marrow examination reveals plasma cells in excess of 30%. Many of them show abnormalities like vacuolation and multinuclearity, such cells are called *myeloma cells.* In advanced cases bone marrow aspirated from any site will reveal the abnormality. If in doubt, aspiration from a site showing radiological abnormality will be diagnostic (Fig. 23.36).
2. Detection of increased levels of abnormal globulins in blood demonstrable as myeloma band also called monoclonal band (M-band), on serum electrophoresis. Further characterization of the abnormal protein is by immuno electrophoresis (Fig. 23.37).
3. Radiological abnormalities of bones are very common and characteristic. In most of the cases, these consist of punched out multiple defects or confluent areas of rarefaction, seen in the skull, pelvis, vertebrae and other bones. Unlike as in bony secondaries, the serum alkaline phosphatase is not elevated
4. In 50% of cases urine may show Bence–Jones proteins. Myeloma in which the secretory proteins are not detectable is called non-secretory myeloma.

INVESTIGATIONS FOR POLYCYTHEMIA

Polycythemia should be suspected when heamoglobin level is > 16 g/dL and PCV is > 51% in males, and hemoglobin level >15.5g /dL and PCV > 48% in females. Polycythemia may be relative (normal red cell mass) or absolute (increase in the red cell mass). Absolute polycythemia may be primary as in polycythemia vera (PV) or secondary as in chronic pulmonary disease, heavy smoking, high altitude,

congenital cyanotic heart diseases, and renal and hepatic tumors) WHO criteria for diagnosing PV

Major

1. Hemoglobin levels of 18.5 or 16.5 g/dL or above in the males and females respectively or increase in the red cell mass >25% above mean normal predicted values.
2. Presence of JAK2 gene mutation (V617F) or other functionally similar mutations.

Minor

1. Bone marrow hypercellularity and trilineage growth—pan-myelosis (all the elements are increased)
2. Subnormal erythroid levels.
3. EEC (endogenous erythroid colonies):

Diagnosis: Major plus one minor
OR First major plus 2 minor criteria

CHAPTER

24 Hematological Emergencies and their Management

Mathew Thomas, KV Krishna Das

Severe anemia, Agranulocytosis, Bleeding, DIC, Immune thrombocytopenia, Deep vein and thrombosis, Disseminated intravascular coagulation, Severe hemolytic crisis, Macrophage activation syndrome, Immune reconstitution inflammatory syndrome, Transplant rejection syndrome

SEVERE ANEMIA

Hemoglobin less than 5 g/dL complication—cardiac failure.

Treatment packed red cells transfusion or exchange transfusion to raise the hemoglobin to comfortable levels, ideal to raise it to 10g/dL or more

AGRANULOCYTOSIS

Suspect the disease if there is severe throat pain, necrotic ulcerations in the mouth, high fever or toxemia in any patient receiving drugs.

Treatment: Withdraw the offending drug forthwith and start strong bactericidal antibiotics like gentamicin, carbenicillin, cefotaxime, ceftazidime or amikacin. Transfusion of fresh blood is a much less efficient alternative. Use of colony stimulating factors should be considered in many cases it is beneficial.

BLEEDING

Institute local measures to arrest bleeding. In coagulopathies, local application of gelfoam or other styptics may help. Identify the possible causes by preliminary tests and administer the necessary clotting factor parenterally.

Calculation of dose of antihemophilic globulin (AHG) in hemophilia. Desired percent increase in factor:

Dose of AHG requires = Desired increased of factor VIII % × wt in kg.

If pure AHG is not available, cryoprecipitate can be given as an alternative. As far as possible the patient or his near-relative should be trained to take self-injection at the earliest sign of bleeding. If both are not available fresh frozen plasma (FFP) is a less efficient alternative.

IMMUNE THROMBOCYTOPENIA

High dose steroids, large doses of IV immunoglobulin, platelet transfusion and emergency splenectomy may be life-saving.

Deep vein thromobosis (DVT): The condition is serious due to the risk of fatal pulmonary embolism. DVT should be prevented by appropriate anticoagulation in all predisposed conditions. Once DVT occurs active treatment has to be instituted to prevent its spread and embolization.

After confirming the diagnosis of DVT, heparin should be started in the acute phase. Currently low molecular weight heparin (LMWH) is the drug of choice which should be given twice daily as subcutaneous injections, e.g. enoxaparin 1mg/kg twice daily if renal functions are normal. Oral anticoagulants like warfarin should be started as early as possible along with heparin in a dose 5 to 10 mg daily. The dose should be adjusted to reach a target INR of 2 to 3. At this point heparin may be stopped. The oral anticoagulant is continued for 6 months to one year is 300 to 500 units/kg body weight are given as IV infusion continuously.

Disseminated intravascular coagulation (DIC): Identify and remove the cause. Heparin in small doses and replacement of fibrinogen and clotting factors (fresh frozen plasma) help to arrest the intravascular coagulation and restore coagulability of blood. DIC is a hematological emergency with high mortality. The basic treatment of DIC is the treatment of the underlying cause. Supportive treatment includes control of hemodynamic parameters, respiratory support and sometimes invasive surgical procedures. Control of bleeding and thrombocytopenia should be undertaken with blood component therapy including FFP, cryo-precipitate and platelet concentrates. Clotting factor concentrates are not recommended.

SEVERE HEMOLYTIC CRISIS

This may complicate several underlying diseases such as falciparum malaria, sickle cell anemia, anaerobic infections, poisoning, snake bites, paroxysmal nocturnal hemoglobinuria, autoimmune hemolytic anemia, cancer, Rh incombatatility and others. Severe hemolysis leads to rapid development of anemia, hemoglobinuria, dysfunction of vital organs such as the kidneys, heart and brain and if untreated, the condition is fatal.

Principles of treatment include:

1. Attention to the primary cause.
2. Correction of anemia by most compatible red blood cells.
3. Prevention of renal failure and maintenance of vital functions. Several drugs are available to allay the hemolysis.

MACROPHAGE ACTIVATION SYNDROME

This is rare and potentially fatal disorder which is thought to result from uncontrolled activation and proliferation of T-cells and excessive activation of macrophages leading to macrophage activation syndrome (MAS). This may complicate infections, malignancies and inflammatory diseases such as juvenile idiopathic arthritis.

The patients present with nonremitting high fever, lymphadenopathy, hepatosplenomegaly, pancytopenia, liver dysfunction, low ESR, hypertrigly ceridemia and hyperferritinemia, coagulopathy and CNS dysfunction. Diagnosis is supported by the finding of well differentiated macrophages phagocytosing hemopoietic cells in the bone marrow. The mortality is high ranging from 15 to 60%. Aggressive treatment includes supportive measures and immunosuppression with high doses of steroids, intravemous immunoglobin, cyclosporine, other immunosuppresents and plasmapheresis.

IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME

With the institution of antiretroviral therapy in HIV infection and AIDS, immune status of the patient improves and opportunistic infections are successfully overcome. But a small number of patients develop inflammatory disease in response to specific opportunistic pathogens within a few weeks or months of initiating therapy. This exuberant inflammatory response is called immune reconstitution inflammatory syndrome (IRIS).

It presents as exacerbation of a partially or completely treated opportunistic infection, especially tuberculosis and other mycobacteria. The clinical manifestations in patients who develop TB IRIS include high fever, new or worsening lymphadenopathy, exacerbation of pulmonary lesions and new or increasing pleural effusion. Non-pulmonary presentation includes expanding central nervous system lesions, skin or visceral abscesses, bony lesions or hypercalcemia.

The principles of treatment include continuation of the current ART regimen and if indicated, anti-inflammatory medications (NSAIDs and corticosteroids) to suppress the inflammatory process.

TRANSPLANT REJECTION SYNDROME—GRAFT VERSUS HOST DISEASE

This is a serious and devastating problem developing in 10 to 80% of transplant recipient especially bone marrow transplants. Graft versus host disease (GVHD) occurs as a result of graft versus host immune reaction in which the host rejects the graft which undergoes damage and death. This process may be acute occurring within 4 to 8 weeks, or chronic starting after 12 weeks and extending over several months or even years. Main targets of attack are the immune system, the skin, GI tract, liver and brain. The GVHD is prevented by continuous immune suppression therapy. Aggressive treatment is needed to save life in severe cases.

SECTION

9

Endocrinology

CHAPTER

25 General Considerations

KP Paulose, KV Krishna Das

Anatomy and functions of endocrine organs, Pattern of endocrine disorders in India, Genetically determined endocrine abnormalities, Paraneoplastic manifestations of malignancy

INTRODUCTION TO ENDOCRINOLOGY

Endocrine glands are ductless glands which secrete hormones. They provide important regulatory influences on cellular metabolism.

Hormones have different sites of action. Many act on the target tissues often distant from their glands of origin—endocrine action. Some hormones act on cells adjacent to their site of origin—paracrine action, while others act on their own cells of origin—autocrine action. Resistance to hormone action can involve any or all of those pathways. Several endocrine glands can be involved simultaneously resulting in hypersecretion of the hormones as in multiple endocrine neoplasia—MEN syndromes. So also hypofunction of multiple glands occurs in conditions such as autoimmune polyglandular syndromes.

Endocrine disorders fall under different groups, based on their pathogenesis:

1. Those caused by over or under secretion of hormones, e.g. hyperthyroidism, acromegaly, gigantism, myxedema, pituitary dwarfism.
2. Those caused by ectopic production of hormones or related substances, e.g. carcinoma bronchus causing Cushing's syndrome, hypernephroma causing hyperparathyroidism.
3. Disorders due to the unresponsiveness of target tissues to the hormones, e.g. testicular feminization syndrome, pseudohypoparathyroidism, thyroid hormone resistance syndrome, insulin resistance syndrome.
4. Those due to deficiency of enzymes required for the synthesis of a hormone resulting in excess production of intermediate products, alternate products or precursors, e.g. dyshormonogenesis in Pendred's syndrome resulting in hypothyroidism and congenital adrenal hyperplasia with adrenogenital syndrome.
5. Abnormalities caused by heightened tissue susceptibility to hormone action, e.g. hirsuitism in young females with normal androgen levels.

Though previously the pituitary was considered to be the master endocrine gland which controlled the others, with the discovery of releasing and inhibitory hormones secreted by the hypothalamus, the pride of place has shifted to the hypothalamus at present.

ANATOMY AND FUNCTIONS OF ENDOCRINE ORGANS

Hypothalamus

The hypothalamus consists of the subthalamic tegmental region of the brain and structures forming the floor and the anterior part of the lateral wall of the third ventricle.

Hypothalamic Hormones

- Corticotrophin releasing hormone (CRH)
- Thyrotrophin releasing hormone (TRH)
- Gonadotrophin releasing hormone (GnRH)
- Growth hormone releasing hormone (GHRH)

- Growth hormone release inhibiting hormone (somatostatin)
- Prolactin releasing and prolactin inhibiting (Dopamine) hormones
- Melanocyte stimulating hormone releasing factor (MSHRF)
- Arginine vasopressin and oxytocin.

Probably the end organ hormones exert their feedback effects on the hypothalamus as well as the pituitary gland.

Pituitary Gland

This weighs about 0.5 to 1 g. The blood supply is derived from the internal carotid and anterior cerebral arteries. Venous drainage is into the cavernous sinuses. The gland is situated in the pituitary fossa. Below is the sphenoid air sinuses, on either side, the internal carotid arteries and cavernous sinuses. The posterior pituitary is continuous with the pituitary stalk of hypothalamus above.

Hormones

Anterior Lobe

- Thyroid stimulating hormone (TSH or thyrotrophin)—Pulsatile, more at night
- Adrenocorticotrophic hormone (ACTH)—Circadian rhythm
- Growth hormone (GH)—Circadian rhythm, more in the morning.
- Follicle stimulating hormone (FSH)—Pulsatile
- Leutinizing hormone (LH)—Pulsatile
- Prolactin—Pulsatile secretion
- Beta lipotrophins (β-LPH)
- Alpha,beta and gamma endorphins derived from β-LPH.

Intermediate Lobe

Alpha and beta melanocyte stimulating hormones (MSHs).

Posterior Lobe

Mainly arginine vasopressin (antidiuretic hormone—ADH) and oxytocin, both synthesized in the supraoptic and paraventricular nuclei of hypothalamus and migrate as neuroseretory granules to the posterior pituitary.

Thyroid Gland

Weight: 15 to 25 g

Blood supply is from superior thyroid arteries which are branches of the subclavian, and thyroidea ima which arises as a branch of the aorta.

Venous drainage is into superior, middle and inferior thyroidal veins which ultimately join the internal jugular vein.

Hormones

Thyroxine (T_4) and triodothyronine (T_3) (only 20% of total) are produced by the thyroid follicles. Thyrocalcitonin is formed in the parafollicular cells. (C cells) 80% of circulating T_3 is derived from deiodination of T_4 to T_3 in the liver and kidneys.

Parathyroid Glands

They are four in number together weighing about 50 to 120 mg, remaining in close relation to the lateral lobes of the thyroid. Sometimes one or more of these glands may remain in the mediastinum in relation to the thymus. Hormone secreted is parathormone.

Pancreas

The whole gland weighs about 90 g. It contains exocrine and endocrine tissues. The arterial blood supply is derived from the splenic artery and pancreaticoduodenal branches of the hepatic and superior mesenteric arteries. Venous drainage is into splenic, and superior mesenteric veins and then into portal vein. The endocrine tissue consists of the *islets of Langerhans* which consists of alpha, beta, delta, and PP cells. Islets form only 1% of pancreas weight, most of the islets are located in the tail of the pancreas. Insulin secretion per day is approximately 50 units. Main hormones are —Insulin produced by beta cells, glucagon from alpha cells, somatostatin from delta cells and pancreatic polypeptide from PP cells.

Adrenal Glands

These are two in number, right and the left, placed in close relation to the upper poles of the kidneys. Each adrenal weighs about 4.5 g. The cortex forms 90% of the gland. Arterial blood is derived from three suprarenal arteries—superior from inferior phrenic artery, middle from the aorta, and inferior from renal artery. Venous drainage is by suprarenal vein, the right drains into the inferior vena cava and the left drains into the left renal vein.

Adrenal Hormones

Adrenal Cortex

Cortisol, corticosterone, aldosterone, deoxycorticosterone, dehydroepiandrosterone (DHEA) and androstenedione.

Adrenal Medulla

Norepinephrine, epinephrine.

Ovaries

These are two in number. In adults their weight varies with the period of menstrual cycle. Arterial supply is from ovarian arteries which are branches of the aorta. Venous drainage is into the pampiniform plexus from which ovarian veins are formed. The right one drains into the inferior vena cava and the left into the left renal vein.

Hormones

Steroid hormones: 17~ estradiol, estrone (estrogens) pregnenolone, progesterone, 17 (OH) progestone, (progestogens) and androgens like DHEA, androstenedione, testosterone.

Several nonsteroidal hormones are also produced the important ones being relaxin, inhibin and substance P.

Testes

The testes occupy the scrotum from the time of birth in the male. Arterial blood is derived from the testicular arteries which arise from the aorta. Venous drainage is into the testicular veins through the pampiniform plexus. Veins arising from this plexus drain into the inferior vena cava on the right and renal vein on the left.

Hormones consist of testosterone, small quantities of estrogens, small amounts of DHEA, dehydrotestosterone and also androstenedione.

Gut Hormones

The mucosal and muscular layers of the stomach and intestines contain numerous cells which produce hormones with local and distant actions. Together, these are called gut hormones. Paracrine cells release hormones locally, which exert their influence on the neighboring cells.

Neurocrine action is the neurotransmitter function mediated by several of the gut hormones. Some of the peptide hormones like substance P, vasoactive intestinal polypeptide and somatostatin are also formed in neural tissue and such hormones have action on the central nervous system as well as in other tissues.

Their actions are summarized in Table 25.1. Possibly several other substances with hormonal activity exist, which are being identified from time -to-time.

PATTERN OF ENDOCRINE DISORDERS SEEN IN INDIA

Classic diabetes mellitus tops the list in frequency. Though nationwide surveys are not available, limited surveys in different population groups have shown that the prevalence may vary from 6 to 7% among the general population urban 15 to 16%, rural 4 to 5%. Undetected cases and those with impaired glucose tolerance may contribute another equal number. Among the diabetics 96% is type 2 (non-insulin dependent diabetes mellitus—NIDDM) and about 1% is type 1 (insulin dependent diabetes mellitus—IDDM). Malnutrition related diabetes (deleted from WHO classification now) and calcific pancreatitis leading on to diabetes are also seen in several parts of India.

Thyroid disorders are rampant. Several states in India come under the iodine deficiency belt. Therefore goiters, hypothyroidism, autoimmune thyroiditis and goitrous cretinism are widespread. Thyroid carcinoma is also frequent. Among the functional thyroid disorders, Graves' disease and hypothyroidism due to autoimmune thyroiditis are the most frequent.

All other endocrine diseases are encountered from time to time. Among adrenal cortical disorders, Cushing's syndrome caused by adrenal hyperplasia and carcinoma or secondary to pituitary adenoma is common. Incidentalomas which are asymptomatic adrenal masses are also not uncommon. Iatrogenic Cushing's syndrome due to widespread use of corticosteroid drugs, and Cushing's syndrome occurring as a paraneoplastic manifestation of carcinoma lung are seen at times. Primary adrenal cortical insufficiency manifests as Addison's disease. Hypopituitarism caused by several disorders leads to secondary adrenal cortical insufficiency. Adrenal virilism is seen rarely.

Among adrenal medullary tumors pheochromocytomas are the most common. They may arise from the adrenal medulla or other sites. They

Table 25.1: Gut hormones

Name	*Site of production*	*Action*
Gastrin	G cells of stomach and duodenum	Stimulates gastric acid secretion
Cholecystokinin	Brain, duodenum, jejunum	Gallbladder contraction, increased secretion of pancreatic enzymes, it acts as a neurotransmitter in the brain
Secretin	Duodenum, jejunum	Increased secretion of pancreatic bicarbonate
Motilin	Upper small intestine	Stimulates gut motility
Gastric inhibitory Polypeptide (GIP) also known as glucose dependent insulinotropic peptide	Duodenum, Jejunum	Stimulates insulin secretion, decreases gastric acid secretion
GLP1	K cells, ileum, pancreas	Suppresses glucagon, increases insulin secretion
Glucagon and enteroglucagon	Brain, ileum, colon	Leads to hyperglycemia due to increased glycogenolysis
Ghrelin	Stomach, pancreas	Hunger hormone, the counterpart of leptin which induces satiation
Neurotensin	Ileum, adrenals, brain	Vasodilation, inhibits gastric secretion
Somatostatin	Brain, gut pancreas	Inhibits the action of many polypeptides
Vasoactive intestinal polypeptide (VIP)	Gut, central and peripheral nervous system	Stimulation of intestinal and colonic secretion, vasodilatation, and inhibition of acid output
Bombesin	Brain, gut and lung	Stimulates acid secretion, gastrin and pancreatic secretion
Substance P	Central and peripheral nervous system	Vasodilatation stimulates muscle contraction, reduction of rise of plasma glucagons and insulin

are infrequent. They may occur as isolated abnormalities or as part of a multiple endocrine syndrome (MEN II).

Parathyroid lesions are seen not uncommonly. Hypoparathyroidism occurring as a complication of thyroid surgery may present as tetany. Hyperparathyroidism caused by parathyroid hyperplasia or neoplasms gives rise to hypercalcemia and various skeletal abnormalities. Chronic renal failure leads to secondary hyperparathyroidism and osteodystrophy at times.

Vitamin D malnutrition is common in many parts of India, especially in the colder regions in the north. This presents as rickets in children and osteomalacia in adults, particularly in pregnant and lactating women. In addition to the fully manifest cases several milder forms occur, which usually go undetected.

Anterior pituitary disease may present as primary endocrine abnormalities such as hypopituitarism, gigantism and acromegaly or as intracranial space occupying lesions. Hypopituitarism and diabetes insipidus due to viperine snake bite are rare, but specific entities, seen in India. Among diseases affecting the posterior pituitary, diabetes insipidus is the most frequent.

Hypothalamic syndromes are seen at times. These present as classical Froehlich syndrome, obesity, eating disorders or somnolence. Laurence-Biedl-Moon syndrome is also not uncommon with polydactyly and retinitis pigmentosa.

Gonadal abnormalities are widely seen. In males, undescended testes, primary and secondary hypogonadism, azoospermia and impotence are common. In women, delayed puberty, primary amenorrhea, other menstrual irregularities, disorders of breast development, sterility and menstrual disturbances due to polycystic ovarian disease (PCOD) top the list. Postmenopausal osteoporosis is widespread.

Except diabetes mellitus, thyroid disorders and gonadal dysfunction, classical presentation of other endocrine disorders is a clinical curiosity seen in all general medical clinics. More than the florid syndromes, milder grades of dysfunction are encountered. This has to be kept in mind and a high degree of clinical suspicion and careful investigations are necessary to diagnose them.

GENETICALLY DETERMINED ENDOCRINE ABNORMALITIES

Many endocrine diseases which are familial can be attributed to genetic defects. The clinical manifestations are due to defects in target cells (hormone resistance syndromes) or due to deficiency of enzymes required for the synthesis of hormones. Genetic disorders can be divided into:

a. *Cytogenic disorders:* Chromosome abnormalities, e.g. Turner's syndrome (XO), Klinefelter's syndrome (XXY), and Prader-Willi syndrome. (deletion of 15 q 11-13)
b. *Single gene disorders:* For example, panhypopitutarism, insulin resistance with acanthosis nigricans and isolated growth hormone deficiency.
c. *Multifactorial disorders:* In this type, severity of expression is variable and it is modified by other genetic risk factors, environmental factors or both. These disorders reveal familial aggregation without a clear pattern of inheritance. Polyglandular autoimmune endocrinopathies and type 1 and type 2 diabetes mellitus are typical examples. Conditions like congenital adrenal hyperplasia (.6.p. 21-.3), Kallmann syndrome (Xp 22-3), multiple endocrine neoplasia-MEN I and II-(llq 13 and 10q-ll.-2), maturity onset diabetes in the young (MODY) (12q.24) and several others.

PARANEOPLASTIC MANIFESTATIONS OF MALIGNANCY

Endocrine abnormalities can occur in several malignant neoplasms due to secretion of peptide substances with hormonal activity. Different neoplasms produce different types of hormones or active peptides with hormonal activity. These manifestations are not due to metastases. Endocrine manifestations may occur along with or before the clinical manifestations of the primary tumor. Removal of the tumor promptly clears the endocrine abnormalities as well. Such manifestations are included under the general term *paraneoplastic syndromes.*

Examples

Hyponatremia syndrome of inappropriate secretion of antidiuretic hormone (SIADH) due to excess secretion of ADH-like substances resulting in hypervolemia and hyponatremia—This may occur in oat cell carcinoma of the lung and carcinomas of the prostate, pancreas, and adrenal cortex.

Hypercalcemia: May occur not only due to bone metastasis, but also due to secretion of substances with activity similar to parathormone. (PTHPP)—parathormone related peptide. This is seen in carcinomas of breast, lung and kidneys and also in lymphosarcoma.

Hypoglycemia: Due to secretion of insulin-like substances (IgFII–insulin growth factor) or somatomedin is seen in hepatoma, mesothelioma and retroperitoneal fibrosarcoma.

Hyperthyroidism: Increased production of TSH like substances occurs in hydatidiform mole and choriocarcinomas.

Cushing's syndrome: Due to excess production of ACTH and melanocyte stimulating hormone (MSH) may occur in carcinoma lung, pancreatic islet cell tumors, neuroblastoma and adrenal-carcinomas.

Rare causes: Bronchial carcinoid may produce growth hormone or growth hormone releasing hormone (GHRH). Duodenal islet tumors may produce gastrin. Carcinoma of lung and kidney may produce chorionic gonadotrophins.

CHAPTER

26

Clinical Examination in Endocrine Diseases

KP Paulose, KV Krishna Das

General symptomatology, Physical examination, Examination of individual glands, Thyroid gland, Parathyroids, Adrenal glands, Pancreatic lesions, Reproductive system, Abnormalities of the pituitary, Abnormalities of the hypothalamus, Pineal gland

As in the case of all other systems the steps to be followed include:

1. Proper history.
2. Physical examination with special attention to anthropometry. Secondary sexual characteristics and abnormalities of endocrine organs.
3. Correlating the symptoms and signs to make a provisional diagnosis.
4. Planning the appropriate investigations for confirmation.

Though all hormones exert their effect predominantly on a particular tissue, there may be several effects on other tissues as well. For example, the thyroid hormone acts mainly on growth, development and metamorphosis but it has got several actions on cardiovascular system, gastrointestinal system and on the brain. Hence, the clinical features may include general symptoms as well as organ-specific symptoms.

GENERAL SYMPTOMATOLOGY IN ENDOCRINE DISEASES

a. Loss of weight	Diabetes mellitus, thyrotoxicosis, Addison's disease, hypopituitarism
b. Obesity (Fig. 26.1)	Prediabetic state, myxedema, Cushing's syndrome (Fig. 26.2), adrenal tumors,



Fig. 26.1: Nutritional obesity boy (18 years)



Fig. 26.2: Cushing's syndrome. Note truncal obesity and buffalo hump (arrow)





Figs 26.3A and B: Female Addison's disease. *Note:* Pigmentation

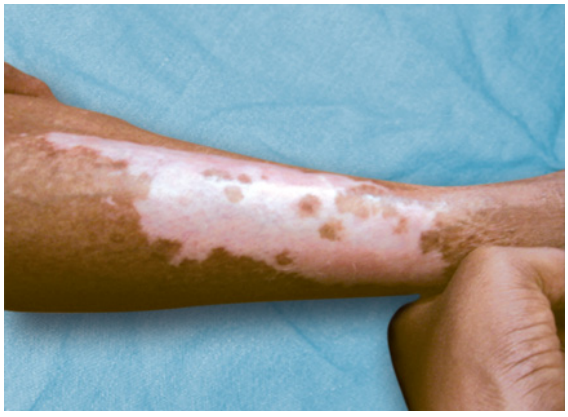


Fig. 26.4: Vitiligo-depigmented patches on the shin

	Froehlich's syndrome, Laurence-Moon-Biedle syndrome
c. Skin pigmentation over axillary folds, palm and sole creases, pressure points, moist surfaces and mucus membranes	Addison's disease (Figs 26.3A and B), Cushing's syndrome, hypothyroidism, thyrotoxicosis
d. Vitiligo (Fig. 26.4)	Hypothyroidism, Addison's disease, diabetes type I
e. Increased sweating (hyperhidrosis)	Hyperthyroidism, hypoglycemia, pheochromocytoma

Cardiovascular Symptoms

a. Dyspnea	Caused by secondary hypertension (pheochromocytoma), obesity (Cushing's syndrome)
b. Palpitation	Thyrotoxicosis, hypoglycemia, pheochromocytoma
c. Edema	Hypothyroidism, Cushing's syndrome, obesity.

Respiratory Symptoms

a. Hoarseness of voice	Myxedema, laryngeal nerve paralysis following thyroid surgery, retrosternal goiter pressing on recurrent laryngeal nerve, carcinoma thyroid
b. Stridor	Hypoparathyroidism
c. Cough when lying down	Pressure on the trachea caused by thyroid and parathyroid tumors.

Gastrointestinal Symptoms

a. Increased appetite	Diabetes mellitus, thyrotoxicosis, pheochromocytoma
b. Anorexia	Hypothyroidism, Addison's disease
c. Increased thirst	Diabetes mellitus, diabetes insipidus, thyrotoxicosis, hyperparathyroidism, hypercalcemia
d. Vomiting	Diabetic ketoacidosis, Addison's disease, pituitary tumors with raised intracranial tension, hyperparathyroidism

e. Diarrhea	Thyrotoxicosis, Addison's disease, diabetic autonomic neuropathy, medullary carcinoma thyroid, hyperparathyroidism
f. Constipation	Hypothyroidism, Addison's disease.

Neurological Symptoms

a. Headache	Secondary hypertension, myxedema, raised intracranial tension
b. Convulsions	Hypoglycemia, diabetic ketoacidosis, hypothyroidism, raised intracranial tension, nonketotic hyperosmolar coma, hyperglycemia
c. Tetany (Fig. 26.5)	Hypoparathyroidism, hypocalcemia, hypomagnesemia
d. Coma	Diabetic coma, nonketotic hyperosmolar coma, hypoglycemia, Addisonian crisis, myxedema coma, pituitary apoplexy
e. Visual disturbances, loss of vision or field defects	Pituitary and hypothalamic tumors, malignant hypertension, transient visual loss in hypoglycemia. Premature cataract should suggest diabetes mellitus and hypoparathyroidism
f. Disturbances of speech	Hypothyroidism Hypoglycemia.

Symptoms Pertaining to Reproductive System

a. Amenorrhea	Panhypopituitarism, prolactinoma, Cushing's syndrome, adrenogenital syndrome, ovarian tumors, thyrotoxicosis, hypothyroidism, ovarian dysgenesis (Turner's syndrome)
b. Galactorrhea	Prolactinoma, hypothyroidism, drugs like chlorpromazine, metoclopramide, digoxin, and H_2 receptor antagonists
c. Hirsuitism	Cushing's syndrome, virilizing adrenal tumors, familial hirsuitism, acromegaly, adolescence, polycystic ovarian disease (PCOD), ovarian tumors like arrhenoblastoma.

Symptoms Pertaining to Urinary System

Polyuria	Diabetes mellitus
Nocturia	Diabetes insipidus
Oliguria	Syndrome of inappropriate secretion of antidiuretic hormone (SIADH).

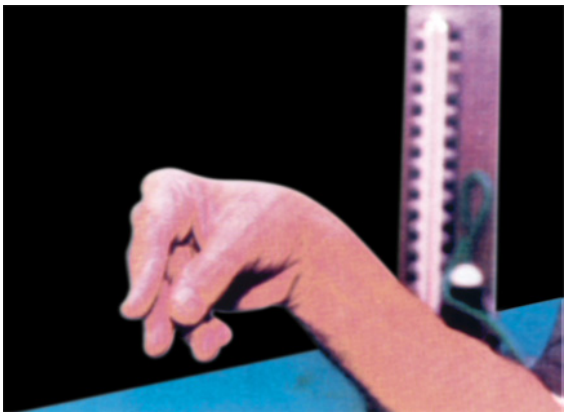


Fig. 26.5: Tetany (Trousseau's sign). *Note:* Accoucher's hand

Past History

Particular attention should be paid to the occurrence of an endocrine disorder, treatment with hormones and surgery on endocrine glands. Past episodes of severe bleeding with shock may lead to pituitary apoplexy and hypopituitarism. So also viperine snake bites may lead to the development of hypopituitarism in later life. The onset of puberty, secondary sexual characters, menstruation, pregnancies or abortions and menopause are all important endocrinological landmarks.

Several endocrine disorders show familial and hereditary predisposition, e.g. diabetes mellitus, hypothyroidism, thyrotoxicosis, multiple endocrine adenomatosis and others. Therefore, it is important to enquire into such diseases in family members.

Environmental factors such as iodine deficiency lead to the development of thyroid disorders. These are very widespread in India. Overdose of iodine in ingested food may give rise to thyrotoxicosis (Jod Basedow's phenomenon). Infections like meningitis may lead to posterior pituitary dysfunction. Mumps occurring in adolescents and adults may lead to orchitis and azoospermia in males and oophoritis leading to sterility in females. Anticancer drugs given in early life may lead to sterility later (cyclophosphamide).



Fig. 26.6: Dwarf normal—age-matched woman for comparison (30 years)



Fig. 26.7: Acromegaly male (45 years) side view. Note the prognatic mandible

PHYSICAL EXAMINATION

Inspection

Stature

A. Dwarfism is shortness of stature below the third percentile for the age (Fig. 26.6). Stunted growth (dwarfism) may be racial or constitutional in some cases. Panhypopituitarism, Laron dwarfism, cretinism, pseudohypoparathyroidism, Turner's syndrome and Froehlich's syndrome are some of the frequent endocrine causes of dwarfism. Infantilism is dwarfism with poor sexual development.

B. The height is increased in gigantism and hypogonadism and Klinefelter's syndrome. In gigantism the height often exceeds 198 cm.



Fig. 26.8: Acromegaly large hands. Note normal for comparison

Anthropometry

At birth the ratio between the upper and lower segments is approximately 1.7:1. By the age of 10 years the ratio becomes 1:1 because the lower limbs increase in length at a higher rate compared to the torso. Hypothyroid dwarfs (cretins) retain infantile skeletal proportions. In constitutional dwarfs and dwarfism due to hypopituitarism the skeletal proportions are not altered. Pituitary hyperfunction producing excess of growth hormone in childhood leads to excessive height and large body size. This is known as gigantism. Maximal linear growth occurs in the bones of the extremities, so that the arm span exceeds the height and lower segment of the body exceeds the upper segment. If growth hormone excess occurs after fusion of the epiphysis acromegaly develops. There is enlargement of the soft tissues and bones of the hands, feet skull and mandible with separation of the teeth (Figs 26.7 and 26.8). In eunuchoidism, the lower segment is longer because of delayed epiphyseal fusion.

Skin and Appendages

Dry, coarse, scaly skin occurs in cretinism and myxedema. Striae over the abdomen, back gluteal region, thighs and other parts develop in Cushing's syndrome (Fig. 26.9). In diabetic ketoacidosis the

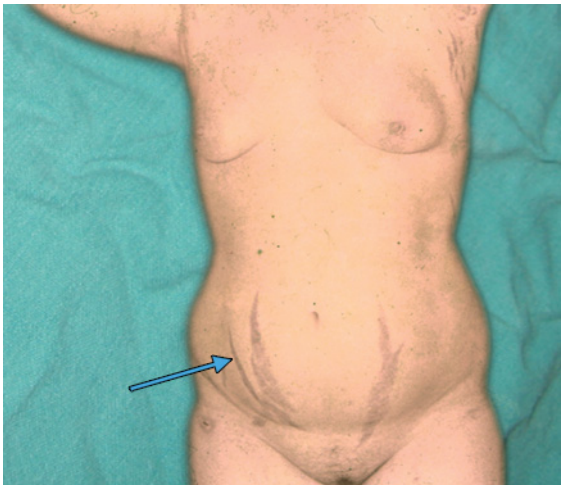


Fig. 26.9: Cushing's syndrome: Striae on abdominal wall (arrow)

skin is dry. In hyperthyroidism the skin is warm and moist. Pretibial myxedema occurs as localized supple cutaneous nodular masses in front of the tibia. Thick woody skin over the nape of the neck (scleredema) may be seen in type II diabetes. Lesions resembling glazed porcelain with yellow or reddish center (necrobiosis lipoidica diabeticorum) and pigmented papules which are usually circumscribed skin spots may be seen in the pretibial region (shin spots) in diabetes mellitus.

Hair

a. Look for the presence, nature and distribution of hair over the face, genitalia, axillae and rest of the body. Hirsuitism is excess growth of hair over moustache area, face, chest and rest of the body in females. Virilizing tumors in women lead to the development of the male pattern of hair distribution.
b. *Absence of body hair in males:* This may be familial at times. Pathologically it occurs in hypogonadism, hypopituitarism and hypoadrenal corticism. Recent fall of body hair occurs in hypothyroidism and hypoparathyroidism.
c. *Abnormality of face:* Moon face or Cushingoid facies—the face is rounded with ruddy prominent cheeks. The ears are hidden behind them. This occurs in Cushing's syndrome.

Eyes

Eyebrows

These are scanty or absent in hypothyroidism (madarosis). This has to be distinguished from lepromatous leprosy which is a common cause of loss of eyebrows. Look for conjunctival congestion, or periorbital edema as in Graves' disease and myxedema, and watering from the eyes (epiphora) in exophthalmos. Infrequent blinking (normal 3–5 times/mt) may be observed in Graves' disease.

Stare

Widening of the palpebral fissure may be normal, familial or congenital. Pathologically it occurs in Graves' disease and in conditions of sympathetic overactivity. Widened palpebral fissure may simulate proptosis.

Lid Lag

Normally, the upper eyelids closely follow the downward movements of the eyeballs, so that the sclera is not visible above the cornea, when the patient looks down. In thyrotoxicosis the upper lid fails to move down fully along with the eyeball, so that a rim of sclera is exposed when the patient looks down. This phenomenon is called lid lag and this indicates thyrotoxicosis. Less commonly this phenomenon may be due to local abnormalities in the eye especially if lid lag is unilateral.

Abridged classification of eye changes in Graves' disease

1. No signs or symptoms
2. Only signs limited to upper lid retraction, stare with or without lid lag and proptosis. No symptoms.
3. Soft tissue involvement leading to excessive lacrimation, edema of conjunctiva and lids (chemosis) and photophobia.
4. Proptosis (Fig. 26.10).
5. Extraocular muscle involvement with restriction, of movements and diplopia.
6. Corneal–ulceration and perforation-exophthalmic ophthalmopathy.
7. Loss of vision due to involvement of the cornea and optic nerve.



Fig. 26.10: Bilateral exophthalmos in a male thyrotoxic patient



Fig. 26.11: Female—thyrotoxicosis with exophthalmic ophthalmopathy

Myasthenia or periodic paralysis may be associated with hyperthyroidism. Myasthenia should be suspected when a patient develops ptosis (drooping) of upper eyelid. In myasthenia, muscle action becomes progressively weak on repetition.

Proptosis (Syn:exophthalmos): Anterior protrusion of the eyeball is called proptosis. The extent of protrusion can be measured by an exophthalmometer. Normal distance from the outer bony margin of the orbit to the apex of the cornea is about 17 mm.

When proptosis progresses, the eyelids fail to cover the eyes. This leads to dryness and ulceration of the cornea. In extreme exophthalmos the extrinsic eye muscles become weak and ineffective and so the eyeball becomes immobile. This is called exophthalmic ophthalmoplegia (Fig. 26.11). Most common cause of exophthalmos is hyperthyroidism.

Generally it is bilateral and symmetrical, less commonly it can be unilateral or asymmetrical. The thyroid dysfunction and ocular abnormalities occur simultaneously in most cases. Less commonly eye signs may precede or follow the thyroid dysfunction. Rarely eye manifestations may be the only abnormality in Graves' disease. This is called ophthalmic Graves' or euthyroid Graves' disease.

Tongue

The tongue should be examined for its size in relation to the mouth, shape, surface, margins, consistency, tenderness and movement. When the tongue enlarges (macroglossia) the speech becomes thick and slurred. Indentation of the teeth are seen at the margins.

Endocrine causes of abnormalities of tongue:

a. *Macroglossia:* Myxedema, cretinism, acromegaly
b. *Microglossia:* Hypopituitarism.

Teeth

Examine the dentition with reference to age. The dentition is delayed in hypopituitarism and cretinism. Several teeth may not erupt. Teeth may be loose in hyperparathyroidism due to resorption of lamina dura of the teeth sockets. Furrows and striations occur on the teeth in hypoparathyroidism. The permanent teeth get separated from each other in acromegaly, due to enlargement of the jaw.

Shape of the Neck

Webbing of the neck is the presence of skin folds on either side of the lower parts of the neck. It is seen in Turner's syndrome.

In Cushing's syndrome, there is accumulation of fat on the dorsal aspect of the lower part of the neck and upper part of the thorax giving rise to a hump-*buffalo neck.*

Lymph Nodes

Rarely lymphadenopathy may be secondary to endocrine diseases. In Graves' disease and Addison's disease generalized lymph node enlargement may be noticed. The upper pretracheal node lying above

the thyroid isthmus—Delphian lymph node may be palpated over the thyroid gland. In carcinoma of the thyroid with secondaries, cervical lymph nodes may be enlarged.

Extremities

Examine the hands and feet carefully. The following abnormalities are of diagnostic importance.

a. *Cretinoid hand:* Short and blunted fingers, square palm and short radius seen in cretinism.
b. *Trident hand:* The fingers are pointed and are of equal length seen in achondroplasia.
c. *Spade hand (syn. Paw hand):* Very prominent thenar and hypothenar eminences with cylindrical spatulate blunted fingers are seen in acromegaly.
d. *Eunuchoid palm:* The palm is long, narrow, with fine skin and delicate, tapering fingers seen in hypogonadism.
e. *Polydactyly:* There are supernumerary digits. This is seen in Turner's syndrome and Laurence-Moon-Beidl syndrome or this may be an isolated abnormality without any accompanying disease.

Nails

The color, surface and texture of the nails should be examined. Various abnormalities like opacities, discoloration, ridging, furrowing, friability, pitting and shedding of the nails may occur in thyroid disorders. Brittle nails are characteristically seen in thyrotoxicosis and hypoparathyroidism. Clubbing of the fingers may occur in thyrotoxicosis.

Generalized Edema

In myxedema there is non-pitting edema. The skin is coarse and dry with sparse hairs. However in secondary hypothyroidism, there is no edema and the skin is thin and shiny.

EXAMINATION OF INDIVIDUAL GLANDS

Thyroid Gland

The term goiter refers to enlargement of the thyroid. Enlargement of thyroid gland can be noticed in front of the neck. In early cases the gland can be seen only when the neck is extended. Classic feature of the thyroid is movement upwards on swallowing. The anatomical relationship of the thyroid gland in between the layers of the cervical deep fascia results in movement of the gland along with the larynx on swallowing. This feature helps to distinguish thyroid from other masses like lymph nodes.

It is ideal to palpate the thyroid gland with the palms and fingers, neck being kept semiflexed and the examiner standing behind. Relaxation of the sternomastoid muscle is essential for the examination to be successful. The gland can be displaced to one side by pressure on the opposite side and this makes the lateral lobe more accessible for palpation. Palpate symmetrically for the lateral lobes and the isthmus. Complete the procedure by palpating the thyroid between fingers and thumb during deglutition.

Normal thyroid may be palpable as a soft movable mass and its movements can be readily detected. Except during puberty and pregnancy, the gland is not prominently visible in normal subjects.

Ascertain the following points during palpation. If the gland is enlarged, whether the enlargement is diffuse or nodular. If nodular, is it a single nodule or are there multiple nodules?

Tenderness: This may be present in acute and subacute thyroiditis. Mild tenderness may occur in carcinoma and also when the gland is highly vascular as in thyrotoxicosis.

Consistency: Ascertain whether the thyroid is soft, firm, hard or woody and whether there are calcified nodules. Is the consistency uniform or varied? Carcinoma and woody thyroiditis are generally hard. Hashimoto's thyroiditis may be hard at times. Iodine deficiency goiter may be soft or firm and multinodular goiters have variable consistency. Adenomas and tense cysts may be firm. In primary thyrotoxicosis the gland is soft and warm or may be firm.

Pulsation: When the thyroid is highly vascular as in primary thyrotoxicosis it pulsates. Increased vascularity generally correlates with hyperfunction. This is associated with *thyroid bruit*.

Lower margin: Palpate the lower margin, particularly when the patient swallows, in order to determine whether the thyroid mass extends down into the mediastinum. Clnically retrosternal extension can be demonstrated by asking the patient to raise both arms above the head for 30 seconds when the neck veins would distend with plethoric appearance of face. When retrosternal goiter leads to pressure

effects it may produce signs of mediastinal obstruction. Percussion over the suprasternal area and manubrium sterni may reveal dullness caused by the retrosternal mass.

Mobility: Majority of goiters are mobile. Mobility is tested by trying to move the gland from side-to-side with the neck kept flexed and turned to the ipsilateral side to relax the sternomastoid. The thyroid may get fixed to deeper structures in malignancy and thyroiditis.

Auscultation

With the patient holding the breath, auscultate over the lateral lobes and isthmus. When the thyroid is highly vascular, continuous bruit may be audible. Thyroid bruit has to be distinguished from aortic stenotic murmurs which may be conducted up to the neck. So also, bruit may arise from the carotid or vertebral arteries. Arterial bruit and the murmur of aortic stenosis are systolic in time. Look for carotid pulsation—absence of pulsation may occur in thyroid carcinoma infiltrating into the neck, but this is a very rare finding. Absence of carotid pulsations is more often due to occlusive arterial disease.

Myxedema jerk: In hypothyroidism, the deep tendon reflexes show delayed relaxation after a normal contraction—it is best demonstrated at the ankle.

Parathyroids

Normally they are found embedded behind the lateral lobes of the thyroid and are not visible or palpable. Less commonly they may be present in the mediastinum in relation with the thymus. In some cases of hyperparathyroidism one or more of the parathyroids may be palpable in the neck. Their position is variable. Careful search should be made to palpate parathyroid tumors in all suspected cases. Mediastinal masses may be demonstrable radiologically. CT scanning visualizes the tumors in most cases.

The term tetany refers to the occurrence of spontaneous twichings and contractions of muscles in part or full caused by hypocalcemia, and less commonly by hypomagnesemia.

Hypoparathyroidism caused by primary parathyroid disease and accidental removal of the parathyroid during thyroid or other neck surgeries also lead to tetany. Presence of tetany can be elicited clinically.

Elicitation of Tetany (Fig. 26.5)

1. *Trousseau's sign:* Apply a sphygmomanometer cuff above the elbow, inflate it above systolic pressure and maintain for 3 minutes. The wrist gets flexed and fingers and thumb become adducted and extended (accoucher's hand).
2. *Chvostek's sign:* Tap with a knee hammer on the side of face 3 to 5 cm below and in front of the ear. The facial muscles twitch briefly with each tap. 5% of the normal population may give a positive Chvostek sign.
3. *Schultz's sign:* Tapping of the center of the tongue with the finger will give rise to local depression due to contraction of the muscles.

Adrenal Glands

These are situated in relation to the upper poles of the kidneys. In infancy and childhood adrenal tumors (neuroblastomas) are common. These assume large sizes and are easily palpable. Clinically they resemble renal masses from which they have to be distinguished by special investigations like ultrasonography and CT/MRI scanning. Adrenal medulla comprises about 10% of the total adrenal mass. In adults usually adrenal tumors are not palpable per abdomen.

In adults, adrenal tumors commonly arise from the cortex. Adrenal cortical hyperplasia involving any of the functional elements—glucocorticoids (Cushing's syndrome) and mineralo-corticoids (hyperaldosteronism) may give rise to small or medium sized tumors. Cushing's syndrome is caused in most cases by bilateral adrenal hyperplasia and carcinoma or adenoma of the adrenal cortex. They may not be readily detectable by palpation. Special radiological procedures, ultrasonography, CT scanning, MRI and isotope scanning are capable of picking up most of them. Their functional status is determined by estimating hormone levels in peripheral venous blood or blood obtained by selective venous catheterization.

Pheochromocytomas may arise from the adrenal medulla or other regions where there is chromaffin tissue such as para-aortic region, urinary bladder or mediastinum.

Endocrine Pancreatic Lesions

The islets of Langerhans comprising less than 1% of the total weight of the pancreas contribute the main endocrine tissue. These contain alpha, beta and pp cells. The alpha cells produce glucagon and beta cells are the source of insulin. Exocrine pancreatic lesions are described in Chapter 5,6 and 7. Usually the endocrine lesions do not produce locally detectable abnormalities by themselves. Lesions such as chronic pancreatitis, especially calcific pancreatitis and hemochromatosis may be associated with diabetes mellitus.

Diabetes developing as a result of lesions in the islet cells contribute the most common endocrine metabolic problem in all countries. The lesions are mostly biochemical. Almost all systems are affected at all stages of diabetes, reversibly in the early stages and irreversibly in the later stages. Diagnosis and management are based on several laboratory investigations which are described in Chapter 27.

Reproductive System

Male Reproductive System

The testes are easily palpable. In intrauterine life up to seventh month the testes are intra-abdominal. They descend into the scrotum from then on to become scrotal organs by the time of birth or even as late as three months postnatally. Failure of descent of the testes is a common abnormality seen in young boys and adults. The testes may be totally intra-abdominal or remain in the inguinal canal. The latter presents as an inguinoscrotal swelling.

In boys normal testis measures 1 to 1.5 cm in size and is just firm. Pubertal changes begin between 10 and 14 years. With the onset of puberty, secondary sexual characters develop and are complete between 15 to 17 years. Pubic hairs start appearing by 11 to 12 years, testicular enlargement starts between 12 and 16 years and the height spurt is maximum between 12 and 15 years. Size of the testes can be measured using a Prader orchidometer.

The normal adult testis measures 2.5 × 3 cm and has a volume of 12 to 25 mL. It is firm to feel. Ninety percent of its bulk is due to seminiferous tubules. Pressure on the testis gives rise to a peculiar sickening sensation which is referred to as the testicular sensation. In tumors such as seminoma and syphilitic gummata, the testes may be enlarged and hard and the testicular sensation is lost. Severe tenderness of the testes occurs in acute or subacute orchitis which is common in filariasis, gonorrhea, mumps and other infections. In testicular atrophy the testes shrink, become soft and may even become impalpable. The most common scrotal lesions seen in India are inguinoscrotal hernias and hydroceles. Hernias are often reducible, whereas hydroceles are not. The former being a purely surgical condition is not discussed further. Hydrocele is the collection of fluid in the tunica vaginalis of the testis. It is a very common manifestation of the obstructive phase of Bancroftian filariasis. Hydrocele presents as ovoid swelling which is tense and cystic. If the fluid is clear, transillumination can be elicited. Hematocele is the collection of blood in the tunica vaginalis.

Examination of the penis: The adult penis is 8 to 12 cm long. The glans, penile urethra, corpora cavernosa and corpus spongiosum can all be palpated distinctly. In hypogonadism the penis is infantile and often less than 2.5 cm long. The urethra can be milked for expressing pus, blood or other secretions. Presence of pus indicates urethritis, most common cause being gonococcal or nonspecific urethritis.

Enquire about erection, its frequency, duration, timing, stimuli required for initiating erection, and ejaculation. In normal subjects, erection may be reflex in nature, mediated by spinal reflexes, or psychogenic, controlled by higher centers and brought on by erotic stimuli. Reflex erection occurs most frequently in the early hours of the morning. For proper erection, hormonal influences (testosterone and gonadotropins), autonomic nervous mechanisms mediated by the S2 to S4 spinal segments and vascular factors which ensure proper blood flow into the corpora cavernosa are essential. *Impotence* is the inability to get proper erection sufficient to perform sexual intercourse.

The common causes of impotence include psychogenic factors (anxiety, depression, feeling of guilt, fear and the like), autonomic dysfunction (diabetes mellitus, spinal cord lesions, drugs) and

vascular occlusion involving the internal iliac and penile arteries.

Priapism: This is defined as an abnormal, painful and sustained erection of penis without sexual desire. It is pathological. In most cases the cause is not endocrine in nature.

Female Reproductive System

At birth the female baby may have prominence of the labia and clitoris caused by the maternal estrogens. In some babies perinatal vaginal bleeding may also occur as a result of withdrawal of maternal estrogens. This subsides in a day or two.

Menarche: In India, the onset of puberty is between 11 and 16 years. Pubic hairs start appearing by 12 years and breast development proceeds between 12 and 15 years. Pubertal changes and secondary sexual characters are determined by estrogens, adrenal sex hormones (androgens and estrogens) and pituitary hormones (gonadotrophic hormone, adrenocorticotrophic hormone and mammotrophic hormone). *Sexual precocity* is the development of secondary sexual characters before the age of 8 in boys and 6 in girls. Onset of menstruation in the female is called menarche. This occurs between the ages of 11 and 16. *Adrenarche* is the term used to denote the onset of secondary sexual characters mediated by the adrenal sex hormones. These include the development of pubic (pubarche) and axillary hair. Thelarche is the term used to denote the development of the breasts (thela-nipple). The first stage of development of the breast is elevation of papillae, followed by further elevation of breast and papillae as a small mound with enlargement of the diameter of the areola. At the mean ages of 12 to 13, the areola and papillae project to form a secondary mound above the level of breast. In the fully developed breast, the papillae appear to be more prominent due to recession of the areola to the general contour of the breast and this occurs by the age of 15 years.

Delay of menarche beyond 16 years is abnormal and this demands investigation to detect abnormalities. Common causes of delayed puberty are malnutrition, hypogonadism, hypopituitarism, therapy with antiestrogenic hormones, sex chromosome abnormalities such as Turner's syndrome (XO) and serious systemic illnesses in early life such as diabetes mellitus, cirrhosis of liver and renal failure.

Menopause or cessation of menstruation occurs between the ages of 45 and 50 years. Complete cessation of periods follows a brief spell of menstrual irregularity. Since the estrogen levels fall, *hot flushes*, also called *hot flashes*, *v*aginal dryness and atrophy of breasts accompany the onset of menopause. Hot flushes may be disabling at times. They come on as sudden attacks or warmth all over the body, accompanied by palpitation, sinking feeling, sweating and a desire to lie down. They pass off spontaneously within minutes to hours.

When the menopause sets in before the age of 40 years it is called premature menopause. This may be due to pituitary failure, (Sheehan's syndrome), ovarian failure or surgical removal of the ovaries.

Sexual Problems

Proper participation by both sexes is absolutely essential for successful performance of the sexual act. Congenial environment, proper understanding between the sexual partners and physical health are the basic requirements for successful sexual intercourse. The frequencies and mode of sexual intercourse vary in different couples. In general, after the fourth decade the frequency comes down gradually. Sudden cessation of libido and impotence in males and frigidity and dyspareunia in females are often due to physical or psychological problems. Frigidity is absence of sexual desire or inability to attain orgasm. **Dyspareunia** is pain during sexual intercourse. While interrogating, details of the sexual act, dyspareunia and the experience of orgasm by the female should be obtained. Frigidity and loss of libido in female are commonly due to psychogenic factors, onset of menopause or due to endocrine disorders like failure of ovarian, pituitary or thyroid functions and several drugs. Dyspareunia may be caused by local lesions such as vaginitis, imperforate hymen, prolapse uterus or cervical ulceration. Often this may also be psychological. Physical examination, appropriate investigations and counseling are integral parts of sex medicine which has become a subspecialty at present.

Examine the external genitalia. Look for the distribution of pubic hair, labia majora and minora, clitoris, vaginal opening and presence of hymen (perforate or imperforate). Clitoromegaly denotes the enlargement of the clitoris. This is seen when there is excessive levels of androgenic hormones as is seen in tumors of the adrenal cortex, androgen secreting tumors of the ovaries or therapy with androgenic hormones.

Further information is obtained by digital and colposcopic examination of the vagina, Changes occurring during pregnancy are given in Chapter 37.

Enlargement of the ovaries and other pelvic organs can be made out by digital examination of the vagina (or rectum in prepubertal girls).

More information can be obtained by examination under anesthesia with simultaneous palpation over the suprapubic region. Sometimes ovarian cysts may reach large sizes, so as to become prominent abdominal masses. They may have to be distinguished from ascites. The length and direction of the uterine cavity can be measured using a uterine sound.

Ultrasonography

Size of the ovaries, presence of pelvic tumors, uterine enlargement, abnormal collection of fluids, and intrauterine masses (especially pregnancy) can be elegantly and noninvasively confirmed by ultrasonography performed per abdomen. Further refinement of the technique is ultrasonography using transvaginal probes or 3D ultrasonography.

Laparoscopy

Laparoscopy is the technique of introducing a laparoscope through a small incision (1–3 cm) after instilling air or pure carbon dioxide into the peritoneum and visualizing the abdominal and pelvic organs directly. Laparoscopy helps to see the ovaries, tubes, presence of Graafian follicles, ovulation, presence of corpus luteum and most of the abnormalities. Interventions using the laparoscope include tubal ligation, surgical procedures such as biopsy and excision of tumors, harvesting the ovum and others. Both ultrasonography and laparoscopy are essential components of any modern gynecological set-up.

EXAMINATION OF THE BREASTS

The breasts should be palpated in both sexes as part of the general examination. Enlargement of the breast in males is called *gynecomastia*. The glandular tissue can be felt as a firm button or disk underneath and around the areola. True gynecomastia is the occurrence of enlargement of glandular tissue. This is due to endocrine causes. *Pseudogynecomastia* is the enlargement of the breasts caused by deposition of fat without increase in glandular tissue. Often this is a part of general obesity. Breast carcinoma is one of the most frequent cancers affecting women. Rarely the male breast also may be the seat of carcinoma.

Gentle pressure on the areola and milking action over the nipples help to squeeze out secretions. Lactation unassociated with the postpartum state or pregnancy is called *galactorrhea.* It may occur as a pubertal change in both sexes. Pathologically it is caused by prolactin—secreting tumors or as a side, effect of several drugs.

Examination of the Breast in Females

With the patient sitting up, the breasts should be inspected for the presence of swellings, dimples, discoloration, eczema around the nipples and other abnormalities such as retraction of the nipple and discharge. Prominent veins may be seen over the breasts during pregnancy and lactation. Then palpate the whole of each breast with the flat of the palm and fingers systematically both in the sitting and supine positions. Common lesions are mastitis, fibroadenoma and carcinoma. Normal breast tissue is soft to just firm in consistency and not tender. Tenderness suggests mastitis or other inflammatory lesions. In *premenstrual tension,* due to retention of fluids and swelling, the breasts may become tender with each menstrual cycle.

If any mass is palpable, look for its position, size, consistency, tenderness, fixity to skin and fixity to deeper tissues. Milk the nipple to detect any discharge. Carefully palpate the regional lymph nodes for enlargement and tenderness.

Hermaphroditism

True hermaphroditism is the condition in which both testes and ovaries are present in the same

individual. *Male pseudohermaphroditism* is the condition where the gonad is the testis, but the genitalia are of the female type. *Female pseudohermaphroditism* is the combination of ovaries and male type genitalia.

LESION OF THE PITUITARY

Endocrine abnormalities involving the pituitary include overproduction or underproduction of hormones, tumor formation and vascular lesions such as pituitary apoplexy leading to sudden loss of function. Lesions characterized by hormonal abnormalities manifest as endocrine disturbances, whereas tumors give rise to signs and symptoms of intracranial space occupying lesions as well. In many cases hyperfunction is associated with hyperplasia or neoplasia of the pituitary. Some tumors do not produce hormones (nonsecretory) and these present as purely intracranial masses. In addition, tumors arising from neighborhood structures may lead to pressure effects on the hypothalamus and pituitary, thereby causing endocrine dysfunction, e.g. cysts of the Rathke's pouch. Tumors detected during routine testing without any symptoms are called *incidentalomas.*

General features caused by space occupying lesions:

1. Increasing size leads to pressure on neighboring structures. Pressure on the optic chiasma leads to bitemporal hemianopia and later, optic atrophy. Cranial nerve palsies may develop.
2. Increased intracranial tension leads to headache, vomiting and papilledema. Neurological defects may occur.

In many cases the tumor may be slow growing taking several years to produce pressure effects. Complications such as hemorrhage, edema or cyst formation lead to rapid enlargement and worsening of the condition even in slow-growing tumors. Enlargement of the pituitary gland leads to enlargement of the sella turcica and erosion of the clinoid processes-which are demonstrable by lateral view skiagrams of the skull. CT scan and magnetic resonance imaging give excellent details.

Microadenomas (less than 1 cm in diameter) in the pituitary may not cause gross enlargement but hormonal dysfunction may be predominant. Tumors more than 1cm in diameter are called macroadenomas.

Hormonal Effects

Overproduction of hormones: Tumors of the pituitary may lead to overproduction of one or more of the trophic hormones. Excess of growth hormone leads to *gigantism* in children and *acromegaly* in adults. *Prolactinomas* lead to impotence, impairment of spermatogenesis, gynecomastia and galactorrhea in men. In women, it leads to galactorrhea, amenorrhea and hirsuitism. ACTH secreting tumors give rise to *Cushing's disease.*

Pituitary Insufficiency

Growth hormone deficiency in childhood leads to *pituitary dwarfism.* In panhypopituitarism all the target glands show hypofunction. The gonads, thyroid and adrenal cortex are affected uniformly or selectively.

In posterior pituitary lesions decreased production of vasopressin leads to *diabetes insipidus* in which large quantities of dilute urine are passed resulting in dehydration.

Syndrome of inappropriate antidiuretic hormone (SIADH) secretion results in retention of fluid leading to dilutional hyponatremia, mental confusion, convulsions, and oliguria. This may occur as a complication of meningitis, use of several drugs like chlorpropamide, carbamazepine and thiazides, pulmonary tumors and several other diseases. With proper treatment of the underlying condition SIADH also resolves.

Abnormalities of the Hypothalamus

These result in inhibition of the releasing hormones with secondary dysfunction of the pituitary and its target glands. Other disorders attributable to hypothalamic dysfunction include psychogenic amenorrhea, anorexia nervosa. Sometimes hyperphagia, obesity, somnolence and deprivation dwarfism.

In diseases of both the pituitary and the hypothalamus the clinical features are predominantly those of the hormonal effects on peripheral tissues. In many, evidence of intracranial space occupying lesion can be demonstrated by appropriate investigations.

Pineal Gland

Interest in this organ has increased during the past three decades. Pineal gland is known to control biological rhythms and its secretion melatonin has been studied in detail. It is also available for therapeutic use at present. Melatonin levels are usually low during day time. These reach peak levels at midnight. Normal melatonin levels in infants range around 325 pg/mL and they fall to 10 to 60 pg/mL in adults.

Pineal gland weighs 120 mg and its lies beneath the posterior border of the corpus callosum between the superior colliculi behind the third ventricle. The size of the gland diminishes and gets clacified as age advances. This is not associated with any functional disturbances.

Pineal tumors (germ cell tumors) cause pressure effects and endocrine disturbances. Pressure effects lead to rise in intracranial tension, internal hydrocephalus, and pressure on the midbrain resulting in dysfunction of the oculomotor nerve and paralysis of upward gaze *(Parinaud's syndrome).*

Endocrine abnormalities (due to pineal gland tumor pressure) include abnormalities of sexual maturation, diabetes insipidus, polyphagia, somnolence, obesity, behavioral disturbances and disturbances in the circadian rhythms of sleep, temperature regulation, mood changes and others.

CHAPTER

27 Investigations in Endocrine Disorders

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General investigations, Estimation of hormone levels, imaging procedures, Fine needle aspiration biopsy, Diabetes mellitus, Thyroid disorders, Parathyroid disorders, Adrenal glands, Anterior pituitary disorders, Gonadal disorders, Posterior pituitary disorders, Appendix-1

INTRODUCTION

The clinical diagnosis of endocrine disorders and their severity have to be supported by investigations. Many cases of subclinical functional defects can be confirmed only by investigations. The process of diagnosis of an endocrine disorder should aim at:

1. Establishing the functional derangement by clinical examination and laboratory investigations.
2. Locating the abnormal organ by imaging techniques such as radiology, ultrasonography, CT scan, MRI, isotope imaging and selective venous catheterization to estimate hormone levels in venous blood draining the particular gland.
3. Establishing the etiological factor and pathological process. It should be ascertained whether an endocrine hyperfunction is due to hyperplasia of the gland, adenoma, carcinoma or ectopic hormone production. This is done by biochemical tests as well histology. Since treatment of endocrine disorders may involve medical measures, surgical excision, isotope administration or external irradiation, all these steps are to be followed according to specific indications.

GENERAL INVESTIGATIONS

Typical examples are given below:

Urine Test

• Presence of glucose in urine (glycosuria)	Diabetes mellitus
• Hypercalciuria—excess loss of calcium in urine	Hyperparathyroidism
• Increase in 17-keto-steroids and ketogenic steroids in urine	Adrenal cortical hyperfunction
• Increase in vanillyl-mandelic acid (VMA), and metanephrines in urine	Pheochromocytoma

Biochemical Tests in Blood

• Hyperglycemia	Diabetes mellitus, Cushing's syndrome, acromegaly, pheochromocytoma
• Hypoglycemia	Overdose of antidiabetic drugs, insulinoma, Addison's disease, panhypopituitarism
• Hypercholesterolemia	Myxedema
• Hypercalcemia	Hyperparathyroidism
• Hypocalcemia	Hypoparathyroidism

• Hypernatremia and hypokalemia	Hyperaldosteronism, Cushing's syndrome
• Elevation of creatine phosphokinase (CPK)	Primary hypothyroidism
• Reduction of C peptide levels in blood	Type I diabetes mellitus

ESTIMATION OF HORMONE LEVELS

This may be done by several methods such as biochemical estimation, radioimmunoassay, ELISA, ECLIA (Electrochemiluminescence Immuno Assay) or others. For hormonal estimation venous blood has to be sent in quantities specified by the laboratory undertaking the test. If it is desired to localize an endocrine tumor such as parathyroid adenoma or pheochromocytoma, collection of blood from the vein draining the suspected organ is done by selective catheterization. Demonstration of high levels of hormone in this sample is proof of hyperactivity of the gland.

Radioimmunoassay (RIA): Introduction of RIA by Berson and Yallow was a landmark in endocrinology, since minute quantities of hormones which could not be detected till then, came under the ambit of the endocrinologist.

By RIA all hormones except some of the hypothalamic hormones can be estimated. The time of collecting the blood should be mentioned, since levels of many hormones show diurnal variation. For example, corticosteroid levels are highest in early morning, growth hormone and levels of prolactin are highest during sleep and insulin levels are highest after a carbohydrate meal. TSH secretion is maximal between 10 PM and midnight When gonadotrophic hormones are estimated, the period of menstrual cycle and the age of the patient should be mentioned.

When drawing blood for estimating serum calcium, the blood should be flowing freely in the vein and compression by tourniquet should be avoided.

IMAGING PROCEDURES

Imaging procedures are employed to locate tumors and other pathological lesions arising from the endocrine glands.

Radiography

X-ray studies are highly useful in demonstrating the effects of hormonal abnormalities and also to delineate endocrine tumors. A few classic examples are described.

Plain X-ray of the lateral view of the skull brings out enlargement of the sella turcica, erosion of the clinoid processes, suprasellar calcification, silver beaten appearance of skull bones, hydrocephalus and others.

Finding	*Interpretation*
• Enlargement of sella turcica and	Enlargement of the pituitary
• Erosion of clinoid processes	Pituitary tumor
• Suprasellar calcification	Rathke's pouch cysts or tumors like craniopharyngioma
• Silver-beaten appearance of the skull bone	Chronic raised intracranial tension
• Enlargement of the skull and separation of sutures	Hydrocephalus occurring at young age
• Pepper-pot appearance of the skull	Hyperparathyroidism

Plain X-ray of the abdomen may reveal adrenal calcification in Addison's disease and pancreatic calculi in chronic fibrocalculous pancreatitis. X-rays of bones show changes such as osteitis fibrosa cystica, erosion of the margins of the phalanges and resorption of terminal phalanges secondary to hyperparathyroidism. Calcification occuring in sustained hypercalcemia can be made out in several tissues. Resorption of lamina dura of the teeth sockets occurs in hyperparathyroidism.

Selective Angiography

This procedure demonstrates the vascular supply of the organs. Venography and cannulation of the draining veins to estimate hormone secretion by the respective endocrine gland are done when the diagnosis cannot be arrived at by other simpler investigations and also to detect the source of hormone production in the case of paired glands.

Ultrasonography

This is a very reliable investigation to locate lesions in the thyroid, ovaries and testes which are easily accessible. Pancreatic lesions, adrenal lesions, and other abdominal endocrine tumors can also be picked up in many instances.

MRI and CT Scanning

These are very reliable investigations to delineate pituitary lesions, suprasellar lesions, abdominal and pelvic endocrine tumors and possible sites of ectopic hormone production such as lung neoplasms.

Magnetic resonance imaging (MRI) offers definite advantages over CT in the demonstration of intrasellar lesions.

Isotope Imaging

This is most often employed in the case of thyroid lesions using ^{131}I or ^{99m}Tc pertechnetate. Both the anatomy and function of the gland can be assessed. Adrenocortical adenomas can be imaged using selenium-75 methyl 19-norcholesterol.^{131}I or ^{123}I meta iodobenzyl guanidine (MIBG) is used to detect pheochromocytoma. Thallium technetium subtraction scanning or imaging with ^{99m}Tc,—sestamibi is employed to detect lesions of the parathyroid.

There are several other imaging procedures which can bring out lesions in various organs. The student should realize that imaging procedures are complementary to biochemical investigations in arriving at the anatomical, pathological and functional diagnosis. Choice of the imaging modality and selection of the appropriate isotope are highly specialized procedures.

FINE NEEDLE ASPIRATION BIOPSY

This is a very useful and widely employed office procedure which can detect the histopathological lesions in the thyroid and testis. Other endocrine organs are less accessible to direct fine needle aspiration cytology (FNAC).

DIABETES MELLITUS

Estimation of plasma glucose level 120 minutes after the usual meal (postprandial blood sugar—PPBS) gives clue to the state of glucose homeostasis. Levels above 140 mg/dL and below 200 mg/dL suggest the possibility of impaired glucose tolerance. Fasting plasma glucose above 126 mg/dL or random blood sugar above 200 mg/dL is also diagnostic of diabetes mellitus. The diagnosis can be confirmed by GTT.

Glucose Tolerance Test

Glucose tolerance test (GTT) is generally performed in ambulatory subjects, since prolonged recumbency impairs glucose tolerance. Smoking should be avoided during the test since nicotine stimulates catecholamine release which raises blood glucose level.

All antidiabetic drugs should be withdrawn three days prior to the test. GTT should not be done in patients with recent illness, surgery or any major stress.

Procedure

The patient must be given his usual carbohydrate diet for 3 days preceding the test (at least 200 g of carbohydrate daily). After fasting for 8 hours, blood sample is collected for glucose estimation (FBS). Then 75 g glucose dissolved in 300 to 500 mL water is given orally. For children the dose is 1.75 g/kg bw. Blood samples are collected at 30, 60, 90, 120 and 180 minutes for glucose estimation. Nowadays a modified GTT is done in which blood glucose level is obtained fasting and at 2 hours after 75 g of oral glucose is administered, only 2 samples are taken.

Urine formed at the time of blood collection is also examined for sugar and acetone. The values are plotted as a graph for comparison with normals.

A single fasting value of plasma glucose level above **126 mg/dL** or a 2 hours postglucose value above **200 mg/dL** can be considered as diagnostic of diabetes mellitus. In asymptomatic patients, at least abnormal values at two hours should be insisted upon to confirm the diagnosis of diabetes mellitus.

The glucose level can be determined in plasma or serum, or in whole venous blood. The values are different, the level in whole blood being lower than that in plasma (Table 27.1).

Indications of GTT

1. Family history of diabetes mellitus.
2. Sudden unexplained loss of weight.

Table 27.1: Criteria for diagnosis of diabetes mellitus and impaired glucose tolerance

Diabetes	*Venous plasma glucose*	*Venous blood glucose*
Fasting	Above 126 mg/dL (>7 mmol/L)	Above 112 mg/dL (> 6.25 mmol/L)
2 hrs after glucose load	Above 200 mg/dL (> 11.1 mmol/L)	Above 180 mg/dL (> 9.9 mmol/L)
*Impaired fasting GT	Below 126 mg/dL > 6.1 mmol/L)	Below 112 mg/dL (> 5.6 mmol/L)
2 hrs after glucose load (IGT)	140-200 mg/dL (7.78-11.1 mmol/L)	128-180 mg/dL (7.1-10 mmol/L)

Note: Fasting plasma glucose above 100 mg/dL but below 126 mg/dL is also abnormal, and this is called impaired fasting plasma glucose.

3. Repeated infections, especially in the genitals or urinary tract.
4. Mothers with overweight newborn babies (babies weighing above 4 kg).
5. Premature cataract (below 50 years).
6. Delayed healing of wounds.

Test for Gestational Diabetes

In pregnancy, a glucose challenge test is first done in the third trimester in patients with a positive family history of diabetes—50 g of glucose is given orally irrespective of whether the patient is fasting or not (glucose challenge test). If plasma glucose is above 140 mg/dL, she is subjected to 0' Sullivan test where 100 g of glucose is given orally in the fasting state. Blood samples are taken in the fasting state, and also 1, 2 and 3 hours postglucose. Plasma, glucose values above 95, 180, 155 mg and 145 mg/dL respectively indicate gestational diabetes. The test is positive if any two values are abnormal.

Estimation of Insulin and C-Peptide

Insulin levels and C-peptide levels in plasma are low in Type 1 diabetes. In Type 2 diabetes the levels may vary according to the stage of the disease. Normal fasting level of C-peptide is 0.3 to 0.50 ng/mL. Detection of antibodies against:

1. Islet cells
2. Glutamic acid decarboxylase-65 (GAD)
3. Endogenous insulin

help to diagnose and assess the severity of Type 1 diabetes. Estimation of C-peptide levels and islet cell antibodies help to distinguish between Type 1 and Type 2.

Glycosylated Hemoglobin (HbA_{1c})

In normal individuals a small proportion of hemoglobin combines with the circulating blood glucose and this fraction is called glycosylated or glycated Hb. This can be separated into 3 types HbA_{1a}, HbA_{1b}, and HbA_{1c}, more binding is to HbA_{1c}.

The proportion of glycosylated hemoglobin increases with increasing levels of blood glucose. The binding of glucose to Hb is a nonenzymatic process that occurs continuously throughout the lifespan of the red cells. Once glycosylated, the elevated levels persist throughout the lifespan of the RBC. The proportion of glycosylated Hb in blood reflects the efficacy of glycemic control during the previous 8 to 12 weeks. Normal level of HbA_{1c} is below 6%. Elevation of HbA_{1c} above this value indicates poor glycemic control. Higher the levels, worse is the control and greater is the risk of complications.

Renal Glycosuria

In this condition there is elimination of glucose in urine, but the blood glucose values are well within normal limits.

Microalbuminuria

For the diagnosis of diabetic state estimation of blood glucose level is adequate. It has been realized that one of the most serious and life-threatening complications, i.e. diabetic nephropathy sets in and relentlessly proceeds at varying rates finally to end up in renal failure and death. By proper management, this can be postponed and its course modified. Therefore, it is important to identify the subjects who develop nephropathy which usually manifests about 8 to 10 years after the onset of diabetes. The earliest indication of the presence of diabetic nephropathy is asymptomatic microalbuminuria. It is associated with retinopathy and neuropathy in many cases.

When the urinary albumin excretion exceeds 30 mg/day but is less than 300 mg/day, this state is called microalbuminuria, since this cannot be detected by the usual side room tests for urinary proteins. Microalbuminuria is tested by RIA or immunoturbidimetric methods. The test is expensive and therefore, it is not done frequently except for assessment of the renal status.

Hypoglycemia

Whipple's triad: Classical hypoglycemic syndrome consists of symptoms of hypoglycemia, plasma glucose levels below 50 mg/dL in men or 45 mg/dL in women, and clinical response to glucose administration. In diabetic patients, glucose levels below 70 mg% is considered as hypoglycemia.

Common Causes of Hypoglycemia

a. Overdose of antidiabetic drugs in diabetics receiving treatment.
b. *Postprandial hypoglycemia:* The glucose level rises transiently after a meal, but then falls to low levels leading to hypoglycemic symptoms before returning to base line. The insulin levels may be increased. Causes include rapid gastric emptying, early stages of type II diabetes or widespread malignant disease. In some, it may be idiopathic. Reactive hypoglycemia can be detected by performing glucose tolerance test extending over 4 hours (extended GTT).
c. *Hypoglycemia due to insulin secreting tumors:* This leads to fasting hypoglycemia and postprandial hypoglycemia. Increased levels of serum insulin, C-peptide and proinsulin in the presence of hypoglycemia, should suggest the possibility of insulin secreting tumor.

The ratio of plasma immunoreactive insulin level (U/mL) to the level of plasma glucose in mg/dL in the fasting state helps to suggest insulin secreting tumors. The ratio in normal subjects is always less than 0.33 while most patients with insulinoma have this ratio above 1.

Glucagonoma

When this is suspected, the level of glucagon can be estimated. Normal values are 50 to 100 pg/mL (up to 200 ng/L).

THYROID DISORDERS

T_3, T_4 and TSH Estimation

Thyroid hormones [tri-iodothyronine (T_3) and tetraiodothyronine (T_4)] and thyroid stimulating hormone (TSH) can be estimated. In primary hyperthyroidism T_3 and T_4 levels are high and TSH level is low. In primary hypothyroidism T_3 and T_4 are low, but TSH is high. In secondary hypothyroidism T_3, T_4 and TSH all are low. A more reliable method is to estimate free T_3 and free T_4 rather than total T_3 and total T_4. This is especially so in pregnancy to diagnose Graves' disease (Table 27.2). *Thyroxine binding globulin (TBG)* is also elevated in pregnancy.

Table 27.2: Normal levels of T_4, T_3 and TSH during different periods of life

	T_3 ng/dL	T_4 µg/dL	TSH µIU/mL
Newborn	32-126	11.8-23	0.8-20.4
3-45 days	50-250	8.2-21.9	
Children (1-10) years	94-269	6.4-15	
Adult	80-200	4.5-12	0.2-5.1
Pregnancy	77-232	7-16.9	Normal

Reverse T_3 will be 5 times more than T_3 in cord blood, but by the first year of life it falls to negligible levels.

Fine needle aspiration cytology (FNAC) of the thyroid is a routine procedure to be undertaken in nodular lesions or diffuse enlargement of the thyroid gland. It is a very reliable method to establish the histological diagnosis. Its diagnostic sensitivity is 80 to 85% and specificity 95%.

Systemic illnesses like uremia, liver disease and severe infections can produce low T_3 or low T_4 without specific involvement of the thyroid gland. This is known as *sick euthyroid syndrome*.

TRH test: Administration of TRH leads to TSH release from pituitary. This response is blunted in hyperthyroidism and exaggerated in primary hypothyroidism. 200 mcg of TRH given IV and TSH is estimated. This test is rarely used at present.

Isotopic Studies

Radioactive iodine uptake (RAIU): The situations where estimation of ^{131}I uptake has a definite role are the following:

1. Patients with subacute thyroiditis T_3 and T_4 levels are high, RAIU is low.
2. In factitious hyperthyroidism T_3 and T_4 are raised and RAIU is low.
3. As a pretreatment measure in patients with Graves' disease, RAIU is employed to calculate the amount of radioactive iodine required for therapy.

Isotope scanning: Oral administration of ^{131}I results in the concentration of radioactivity in the thyroid and the gland can be imaged. From the

Table 27.3: Results of various isotopic tests in thyroid disorders

Disease	RAIU	T_4 (RIA)	T_3 (RIA)	TSH
Graves' disease	H	H	H	L
Iodine deficiency goiter	H	N	N/M	N
Primary hypothyroidism	L	L	L	H
Suprathyroidal hypothyroidism	L	L	L	L
Subacute thyroiditis	L	N/H	N/H	N/L
Factitious hyperthyroidism	L	H	H if T_3 is taken	N/L

N = Normal; H = High; M = Marginal elevation; L = Low

image produced, it is possible to assess the function of various regions of the thyroid. Both hyperfunctioning and hypofunctioning regions can be demarcated. Thyroid scan is one of the most commonly used procedures in nuclear medicine. Now ^{99m}Tc pertechnetate is used for thyroid scanning because of the low radiation dose and shorter interval for imaging after IV injection, compared to ^{131}Iodine (Table 27.3).

Thyroid scanning is useful in:

1. Distinguishing whether a nodule is cold or hot on the basis of isotope concentration
2. Picking out multiple nodules
3. Identifying ectopic thyroid at other sites, and
4. Identifying metastases in thyroid carcinoma by whole body scanning (^{131}I wholy body scan).

Using the same principle and appropriate radiopharmaceuticals, the pituitary, adrenals, parathyroid and pancreas can all be imaged.

Tests for Thyroid Medullary Carcinoma

Serum calcitonin level is estimated. Normal baseline level of serum calcitonin is less than 70 pg/mL. Higher levels should suggest tumor.

Pentagastrin Stimulation Test

Pentagastrin 0.5 mcg/kg bw is given as IV bolus and blood samples are collected for estimation of calcitonin 2, 5 and 15 minutes after injection.

In normal persons, calcitonin levels will be elevated 2 minutes after injection and this returns to normal within 10 to 30 minutes. In patients with medullary carcinoma, not only the baseline calcitonin levels are elevated, but a 20-fold rise above the baseline level will be seen after pentagastrin injection.

PARATHYROID DISORDERS

Estimation of serum calcium and phosphorous, urinary calcium, and radioimmunoassay of parathormone (PTH) are helpful in diagnosing parathyroid disorders. Normal serum calcium level is 8.8 to 10.2 mg/dL (2.2–2.56 mmol/L). Serum calcium levels above 11.6 mg/dL (2.9 mmol/L) denote hypercalcemia.

Hyperparathyroidism

There are three types of hyperparathyroidism—primary, secondary and tertiary. Primary hyperparathyroidism is caused by parathyroid hyperplasia or tumors.

Secondary hyperparathyroidism usually develops in renal failure when there is retention of phosphate with reciprocal lowering of serum calcium. In an attempt to raise serum calcium level, PTH secretion increases, but the secretion remains under feedback control.

If this stimulus for PTH secretion persists for long periods the parathyroids become autonomous and PTH secretion goes on at a high rate irrespective of hyper-or normocalcemia. This state is called tertiary hyperparathyroidism.

Hypoparathyroidism

There are three types of hypoparathyroidism.

1. *Hypoparathyroidism due to deficient secretion of PTH:* This may be primary or secondary to surgery,^{131}therapy, hemochromatosis, Wilson's disease and others.
2. *Pseudohypoparathyroidism:* PTH secretion is normal or elevated but there is lack of target tissue response to the hormone. In addition there are congenital malformations.
3. *Pseudopseudohypoparathyroidism:* In this condition, the somatic features of pseudohypoparathyroidism such as short stature, obesity, round face and short metacarpals are present, but the levels of PTH, calcium and phosphorous remain normal (Table 27.4). These skeletal abnormalities are collectively known as *Albright's hereditary osteodystrophy.*

Radiology: In hyperparathyroidism radiological investigation reveals demineralization of bones. Demineralization is most marked on the radial side of the middle phalanges of the hands. Terminal

Table 27.4: Changes in blood levels of parathormone (PTH), serum calcium, phosphorus and creatinine in various parathyroid disorders

Diagnosis	*PTH*	*Calcium*	*Phosphorus*	*Creatinine*	*Congenital abnormalities*
Primary hyperparathyroidism	H	H	L	N	Nil
Secondary hyperparathyroidism	H	L/N	H	H	Nil
Tertiary hyperparathyroidism	H	H	H	H	Nil
Hypoparathyroidism	L	L	H	N	Nil
Pseudohypoparathyroidism	N/H	L	H	N	Present
Pseudopseudohypoparathyroidism	N	N	N	N	Present

H = High; N = Normal; L = Low

phalanges may be resorbed. Skull shows pepper-pot appearance. Soft tissue calcification may be present. Lamina dura of the teeth sockets disappear.

ADRENAL GLANDS DISORDERS

a. *Estimation of ACTH and plasma cortisol:* High plasma ACTH and cortisol suggests Cushing's disease. Low ACTH with high plasma cortisol suggests Cushing's syndrome (primary adrenal disorders). Seventy percent of Cushing's syndrome is due to pituitary tumor and 15% due to ectopic ACTH producing tumors.

b. In hypopituitarism with adrenal insufficiency both ACTH and plasma cortisol are low. In Addison's disease plasma cortisol is low but ACTH is high.

c. *ACTH stimulation test:* After estimating basal plasma cortisol level and urinary 17 ketosteroids (17 KS) and ketogenic steroids (KGS) over 24 hours, 25 units of ACTH diluted in 100 mL of N saline are given as an IV infusion lasting for over 8 hours. Instead of ACTH, a synthetic compound cosyntropin or synacthen is given now (0.25 mg 1M) and serum samples can be obtained after 30 and 60 minutes. Cosyntropin also stimulates aldosterone. 17 KS and 17 KGS are metabolites of cortical hormones excreted in urine. The plasma cortisol and 24 hours urinary 17 KS and KGS are estimated. In primary adrenal insufficiency there will be no rise. A normal response to ACTH consists of a rise of plasma cortisol of 6 mcg/dL above the basal level (>580 nmol/L). In patients suspected to have congenital adrenal hyperplasia (CAH) estimation of 17 (OH) Progesterone level in blood is recommended. A level above >45 nmol/L confirms the diagnosis.

d. *Dexamethasone suppression test:* This test will help to differentiate Cushing's disease, adrenal adenoma and hyperplasia. In normal individuals, administration of low doses of dexamethasone (0.5 mg 6 h × 3 days) suppresses ACTH secretion from the pituitary leading to diminished cortisol secretion. Urinary 17 KS and 17 KGS fall to 50% or less compared to original levels in 3 to 4 days. If there is no suppression the next step is to administer a higher dose of dexamethasone-2 mg 6 h × 3 days. In ACTH dependent conditions such as adrenal hyperplasia, and Cushing's disease there will be suppression, whereas in tumors which are generally independent of ACTH there will be no change (Table 27.5) in the plasma cortisol level.

Table 27.5: Interpretation of diagnostic tests in hyperadrenocortical states

Test	*Normal subjects*	*Pituitary cause Cushing's disease*	*Adrenal tumor*	*Ectopic ACTH production*
Urinary 17 KGS	Normal	H	H	H
Plasma ACTH	Normal	H	L	H
1 Suppression by dexamethasone 1 mg-screening test	Suppression of plasma cortisol	Nil	Nil	Nil
2 Suppression by 2 mg/day for 3 days	Suppression	Nil	Nil	Nil
1/3 Suppression by 8 mg/day x 2 days	Suppression	Suppression	Nil	Nil

H = High; L = Low

At present a simple screening test is employed to exclude Cushing's syndrome.

Plasma cortisol is estimated at 8 AM after taking 1 mg of dexamethasone during the previous night. If plasma cortisol is less than 5 mcg/dL, Cushing's syndrome is excluded.

e. *Corticotropin releasing hormone (CRH) test:* 100 mcg CRH given IV leads to an exaggerated rise in cortisol and ACTH in 95% of patients with pituitary dependent Cushing's syndrome. The term exaggerated rise refers to a rise of 20% above basal level in cortisol and 50% above basal level in case of ACTH.

f. *Inferior petrosal sinus sampling:* Bilateral simultaneous inferior petrosal sinus blood sampling with measurement of ACTH levels in central and peripheral blood in the basal state and following IV injection of 100 mcg CRH helps to differentiate between pituitary dependent and ectopic disease. A central to peripheral ratio of >2 before CRH administration and >3 post CRH is very suggestive of pituitary dependent disease.

Cortical adenomas can be localized also by imaging with selenium-75 methyl 19 norcholesterol.

Adrenal Medulla

Pheochromocytoma: Catecholamines in blood and their degradation products *vanillyl mandelic acid* (VMA), *metanephrines* and *free catecholamines* in urine can be estimated. They are considerably increased in pheochromocytoma. Articles of food like bananas and many drugs increase the excretion of VMA. Such foods, coffee, nicotine, exercise and certain drugs should be avoided for a week before the test. Urine is collected for 24 hours into bottles containing acid, and the total catecholamines are estimated. Plasma catecholamines above 2000 pg/mL are diagnostic.

Suppression Tests

1. *Phentolamine test:* Phentolamine is an alpha adrenergic blocking agent. 2.5 mg of phentolamine is given intravenously. Normal response is suppression of plasma catecholamines after 10 minutes, but in pheochromocytoma plasma levels increase.
2. *Clonidine suppression test:* This test differentiates pheochromocytoma from essential hypertension in patients exhibiting high plasma norepinephrine levels. When 0.3 mg of clonidine is given orally, it will suppress norepinephrine to the normal range within 3 hours in essential hypertension. Failure of suppression is suggestive of a tumor.

Since pheochromocytomas may arise from the adrenal medulla (90%), or other sites of chromaffin tissues, they have to be localized prior to surgery. This is done by CT scan or imaging with ^{131}I *metaiodobenzyl guanidine (MIBG).*

GONADAL DISORDERS

Indications for investigating gonadal functions.

I. Delayed puberty and precocious puberty in boys and girls.
II. Sterility—in women the ovulatory cycle can be monitored by clinical and hormonal studies. In men spermatogenesis can be assessed by performing sperm counts and study of sperm morphology in semen. Normal sperm counts range from 20 to 200 million/mL.

Gonadal Dysfunction

In women the cause of ovarian failure, whether it is primary or secondary to gonadotrophin deficiency, can be assessed by estimating the ovarian hormones—estrogens, progesterones, and the trophic hormones—FSH and LH. The same principle applies to men also. In men testosterone can be estimated. In primary gonadal failure the levels of gonadal hormones will be low and the trophic hormones will be increased. Administration of trophic hormones fails to stimulate the gonads. In gonadal failure secondary to anterior pituitary disease, the levels of trophic hormones and that of the gonadal hormones are all low, but on stimulation with the trophic hormones the gonads respond.

Tumors Arising from the Gonads

Virilizing or feminising tumors may arise from the gonads and adrenal cortex. Estimation of the gonadal hormones and adrenal sex steroids and their metabolities is indicated in such cases.

Biopsy Procedures

Testicular biopsy is a common procedure employed to study the histology of the organ and degree of maturation of sperms. Apart from testicular tumors,

testicular biopsy is done to determine the cause of azoospermia.

Histological examination of the endometrium obtained by cervical dilatation and curettage (D and C) is a very common investigation employed in gynecological practice.

Ultrasonography and Laparoscopy

The production of Graafian follicles and ovum can be determined by ultrasonography and laparoscopy. The latter is employed also for the collection of ovum for use in assisted pregnancy.

Surgical Investigations

In the investigation of sterility in both sexes, tests to determine the patency of vas deferens and fallopian tubes are undertaken routinely.

Karyotyping

When somatic features suggest the possibility of Turner's syndrome or Klinefelter's syndrome, examination of buccal smear for sex chromatin, demonstration of Barr bodies in neutrophil leukocytes and karyotyping help to establish the diagnosis.

Detailed investigation of gonadal hormonal dysfunction, study of the effect of the pituitary trophic hormones on the gonads, methods to stimulate the maturation and liberation of the ovum in the female and sperm in the male and laparoscopic and other procedures for ovum collection, *in vitro* fertilization implantation into the uterus and several other procedures are employed in fertility assistance departments.

ANTERIOR PITUITARY DISORDERS

Nearly all pituitary tumors are benign adenomas, of which 25 to 30% are hormonally silent. Prolactinoma is the most common among the hormone secreting tumors. The following investigations are undertaken to assess the abnormalities of the gland.

Hormonal Studies

a. Estimation of the basal levels of pituitary hormones and the hormones of the target glands: thyroid, adrenal cortex and gonads.
b. Studying the effect of the hypothalamic releasing and inhibiting hormones on release of the trophic hormones from the anterior pituitary and corresponding effects on the target glands.
c. Study of the inter-relationship between the target glands and the pituitary. For example:
 i. Dexamethasone suppression test for pituitary—adrenal relationship.
 ii. Hypoglycemia resulting from administration of insulin stimulates production of growth hormone (GH). Rise in blood sugar inhibits GH secretion. In fact, GH deficiency is diagnosed when the serum level of GH is less than 5 mcg/L in response to insulin induced hypoglycemia.
 iii. The antiestrogen drug clomiphene can be used for studying the relationship between the pituitary and the gonads. When clomiphene is given in a daily dose of 3 mg/kg (maximum 150 mg) for 10 days, it stimulates the release of GnRH from the hypothalamus, which in turn, results in release of LH and FSH from the anterior pituitary.
 iv. Growth hormone suppression test—if growth hormone level is less than 2 mcg/dL 60 minutes after 75 g of oral glucose, acromegaly can be excluded.

Gonadotrophin Releasing Test

Administration of gonadotrophin releasing test GnRH in normal subjects leads to a prompt increase in levels of LH and FSH. This test is used to assess LH and FSH secretory reserves in the pituitary and does not *per se* diagnose gonadotrophin deficiency. 100 mcg of GnRH is given IV and blood samples are collected at 20 and 60' later for estimation of LH and FSH.

Insulin Tolerance Test

Insulin induced hypoglycemia is a powerful stimulus for cortisol and GH secretion. This test is done in suspected hypothalamic—pituitary dysfunction.

Take basal blood samples for glucose, cortisol, ACTH and GH at 9 AM. Soluble insulin is given as an IV bolus at a dose of 0.15 u/kg. Further blood samples are taken at 20, 30, 45, 60, 90 and 120 minutes. Blood glucose will fall to 40 mg% at 45 minutes and patient develops symptoms of hypoglycemia. Rise of cortisol above 500 mmol/L and GH 720 mu/L indicates normal response.

Oral Glucose Tolerance Test in Acromegaly

Growth hormone (GH) secretion is pulsatile. Basal GH concentrations are undetectable most of the time and hence dynamic tests are preferred. Normally glucose suppresses GH secretion. In acromegaly GH levels are paradoxically increased by glucose. The test is done as follows:

Basal plasma sample is taken to estimate GH and glucose. About 75 g of oral glucose is administered. Further blood samples are taken at 30, 60, 90 and 120 minutes and GH and glucose are estimated.

Suppression of GH to less than 1 mu/L excludes the diagnosis of acromegaly.

Triple bolus Injection: Synthetic analogs of three hormones—insulin, GnRH, and TRH are injected as a bolus to stimulate the anterior pituitary gland. The response is assessed by measuring cortiosol, GH, prolactin, TSH, LH and FSH levels in blood. This test was first introduced in 1973. Blood glucose levels are also monitored for hypoglycemia.

Imaging Procedures

Demonstration of the enlargement of the pituitary by imaging techniques. For example:

1. Lateral view radiograph of skull may show enlargement of sella turcica and erosion of clinoid process.
2. Calcification above the sella may suggest calcified cyst arising from the Rathke's pouch. CT scanning and MRI elegantly bring out all.

POSTERIOR PITUITARY DISORDERS

Diabetes Insipidus

Urine osmolality remains below 300 mOsm/kg in pituitary diabetes insipidus (PDI) as well as in nephrogenic diabetes insipidus (NDI). The corresponding urine specific gravity ranges from 1001 to 1005. To differentiate PDI from NDI, urine and serum osmolality are measured after 10 to 25 mcg of desmopressin intranasally or 1 to 2 µg IM. In PDI the urine osmolality will be raised by more than 50% while there is no significant rise in NDI.

Water Deprivation Test

Subjects with obsessive compulsive drinking (OCD) pass large volumes of urine with low osmolality (100–200 mOsm/kg). This can be distinguished from diabetes insipidus by the water deprivation test. Deprivation of fluids for eight hours raises urine osmolality in OCD, but not in PDI and NDI. Severe cases of diabetes insipidus may not tolerate water deprivation for this period and in them the test may have to be interrupted, Both desmopressin injection and water deprivation test can be done simultaneously.

Syndrome of Inappropriate Secretion of Antidiuretic Hormone

Syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is a common cause of hyponatremia. It is associated with hypotonic plasma < 270 mOsm/kg), urine osmolality more than 300 mOsm/kg and excessive renal sodium loss (>50 mmol/L).

Water Load Test

When a water load of 20 mL/kg body weight is gIven to normal persons, 80% of this volume will be excreted within 5 hours and the urine osmolality falls below 100 mOsm/kg (the specific gravity falls below 1005). In SIADH the excretion of the waterload is impaired considerably. There is dilutional hyponatremia as well.

APPENDIX-1

Normal Values in Endocrinology

Anterior pituitary		
• Growth hormone (basal)	GH	4-6 ng/mL
Gonadotrophins (plasma)		
• Premenopausal women except at ovulation	FSH	5-20 mIU/mL (5-20 u/L)
	LH	5-25 mIU/mL
• Ovulatory surge	FSH	12-30 mIU/mL
	LH	25-100 mIU/mL
• Postmenopausal	FSH	> 50 mIU/mL
	LH	> 50 mIU/mL
• Men	FSH	6-18 mIU/mL
	LH	5-20 mIU/mL
• Children of both sexes (prepubertal)	FSH	< 5 mIU/mL
	LH	< 5 mIU/mL
• ACTH at 8 AM		< 80 pg/mL
• Thyrotropic hormone TSH (RIA)		< 5 μIU/mL
Prolactin (Plasma)		
• Nonpregnant women		2-15 ng/mL
• Pregnant women		150-200 ng/mL
Posterior pituitary		
Oxytocin		
• Men and preovulatory women		0.5-2 μIU/mL
• Lactating women		5-10 μIU/mL
Adrenal cortex		
• Aldosterone in upright position and normal diet 8 AM		< 8.5 ng/dL
Cortisol at 8 AM		5-25 μg/dL
at 4 PM		3-10 μg/dL
• 17 (OH) corticosteroids in urine		2-10 mg/day
• 17-Ketosteroids in urine	men	7-25 mg/day
	woman	4-15 mg/day
Adrenal medulla		
• Free catecholamines in urine		< 100 μg/day
• Epinephrine in urine		< 25 μg/day
• VMA in urine		< 8 mg/day
Gonadal hormones		
• Estradiol in plasma		
Premenopausal women		20-360 pg/mL
Postmenopausal women		< 30 pg/mL
Men		< 50 pg/mL
• Progesterone in plasma		
• Men, prepubertal girls, preovulatory periods, and postmenopausal women		< 2 ng/mL
• Women—leuteal peak		> 5 ng/mL

- Testosterone in plasma (morning sample) — range up to 21 ng/mL
 - Male: 300-1000 ng/dL
 - Female: < 100 ng/dL
 - Prepubertal boys and girls 5-20 ng/dL

Thyroid

Tri-iodothyronine T_3 (RIA)	70-190 ng/dL
Tetraiodothyronine T_4 (RIA)	5-12 µg/dL
Free T3	2-4.5 pg/mL
Free thyroxine	2-4 ng/dL
Thyrogolobulin	0-60 ng/mL

Other hormones

1. Angiotensin II in plasma 8 AM	10-30 pg/mL
2. Calcitonin in plasma	<50 pg/mL
3. C-peptide (fasting)	0.3-3.7 ng/L
4. Gastrin in plasma	<120 pg/mL
5. Glucagon in plasma	50-100 pg/mL
6. Parathormone	10-60 pg/mL
7. Plasma insulin (fasting)	6-26 µ/mL

Note: IU = International units

SECTION

10

Nephrology

CHAPTER

28 General Considerations

R Kasi Visweswaran

Applied anatomy, Applied physiology, General patterns of medical disorders affecting the kidneys and urinary tract in India

INTRODUCTION

Advances in the understanding of the excretory system in health and disease over the last five decades have led to newer modalities of treatment. Conditions which were considered to be invariably fatal, such as chronic renal failure can be managed now by renal replacement therapy in the form of maintenance dialysis or renal transplantation. Since chronic kidney disease is a progressive illness, high index of suspicion, early diagnosis and prompt management are extremely important. In this chapter, the steps for an adequate clinical evaluation of a patient with diseases of the excretory system are described. A patient with disease of the kidney or urinary tract may present in several ways:

1. Remain asymptomatic with normal urine tests.
2. Remain asymptomatic with abnormalities in urine detected by investigations.
3. Have symptoms directly referable to the excretory system and showing abnormalities on investigations.
4. Present with renal or non-renal manifestations of a generalized disease like diabetes mellitus or dyscollagenosis which commonly affects the kidneys as well.

APPLIED ANATOMY

The kidneys measure about 11× 6× 3 cm and weigh 125 to 170 g. They occupy the retroperitoneal space on either side of the vertebral column from D_{12} to L_3 vertebrae with the upper poles nearer to the midline. The right kidney is lower than the left by 1.5 cm because of the liver above it. The upper pole of the left kidney reaches the transverse process of D_{11} vertebra. Kidneys are placed in close apposition to the diaphragm. During respiration, the kidneys move only 1 to 2 cm in the vertical axis since the movement is restricted by the perinephric fascia. Upper part of the medial border and the anterior aspect of the upper pole are in close apposition with the corresponding suprarenal gland. Normal kidneys are not palpable in well built or obese adults. But in thin subjects, the lower poles of both kidneys may be palpable during deep inspiration. Being retroperitoneal organs, the enlarged kidneys are better palpable bimanually, especially by the hand placed posteriorly in the loin below the 12th rib, just outside the lateral margins of the paraspinal muscles. Enlargement of the suprarenals may cause downward displacement of the kidney. Gross enlargement of the suprarenal may mimic renal enlargement clinically. Renal enlargement is often due to cystic diseases, obstruction or tumors. Common renal tumors in childhood such as nephroblastomas and neuroblastomas are large tumors.

Developmentally the kidneys are mesenchymal in origin and are formed from the metanephros. From their initial position in the pelvis they ascend into the abdomen. Failure of ascend results in the presence of the kidneys in the pelvis or at any site below its normal position. Horseshoe kidney is a rare congenital anomaly in which the lower poles of both kidneys are fused across the midline in

front of the vertebral bodies and aorta. The ascent is arrested by the origin of the inferior mesenteric artery arising from the abdominal aorta. The lower poles may be connected by functioning renal tissue or fibrous bands. Other common developmental anomalies include agenesis of kidneys, variation in the number and branching pattern of renal arteries and veins, double pelvis and ureters, incompetent vesico-ureteric junction, ectopic opening in ureters and the presence of posterior urethral valve.

The kidney receives its blood supply through the renal artery which arises from the aorta. Even in normal persons, there can be more than one renal artery supplying the kidney. Similarly, renal veins may be single or multiple and they drain into the inferior vena cava. The lymphatics drain into nodes alongside the aorta and inferior vena cava. Auto-nomic nerve supply is derived from the renal plexus which is formed by branches from the coeliac and aortic plexuses.

Surface Projection of the Kidney

The kidney can be marked at the back within the Morrison's parallelogram which is drawn as given below (Fig. 28.1). Two horizontal lines are drawn at the spines of T_{11} and L_3 vertebrae. Two vertical lines are drawn 2.5 cm and 9 cm from the midline. The center of the hilum corresponds to the lower border of first lumbar vertebral spine.

Since the kidneys lie immediately anterior to the lower ribs and the muscles of the posterior abdominal wall with no vital structure interposed between them, this approach is preferred for exposing the kidney for surgery, needle biopsy. Percutaneous placement of nephrostomy tubes into the dilated collecting system and percutaneous stone removal, i.e. percutaneous nephrolithotomy (PCNL).

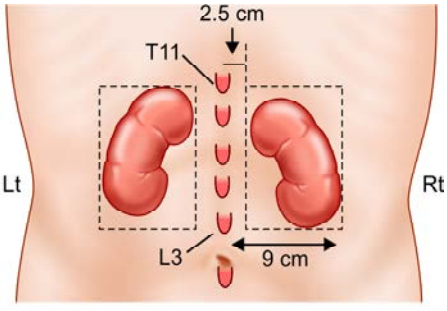


Fig. 28.1: Surface projection of the kidney on the back

Normal Drainage of Urine

Urine formed in the kidneys is drained into the renal pelvis and it passes down the ureters which are 20 to 25 cm long and 5 mm wide. The ureters descend along the tips of the transverse processes of the lumbar vertebrae to enter the bladder at the trigone after a short oblique course through the detrusor muscle. This oblique intramural course and sling-like arrangement of the muscles act as a sphincter and prevent the backflow of urine into the uteters during micturition when the bladder pressure increases *(vesicoureteric reflux)*.

Normal adult urinary bladder can usually hold up to 500 mL of urine. In chronic obstruction, it may dilate and become more voluminous. When distended, it can be seen or felt in the suprapubic region as a globular swelling.

In normal persons, infection of the bladder is prevented by the flushing action caused by complete emptying of the urinary bladder during micturition and the presence of the normal constitutents of urine such as urea, Tamm-Horsfall proteins and prostatic secretions. The protective mucus coating of the bladder mucosa prevents bacterial adhesion. Obstruction to the urinary tract, instrumentation, catheters or other foreign bodies like stones and abnormal physicochemical composition of urine can alter this normal defence mechanism and predispose to infection. The infection establishes itself in the urinary tract when the organism gets an opportunity to adhere to the mucus membrane. Some bacteria like *E.coli* have fimbriae on their surface with which, they get attached to the mucosa even if the urinary tract is structurally normal. Other bacteria like *Klebsiella* tend to colonize only if the urinary tract is structurally abnormal or it contains foreign bodies.

APPLIED PHYSIOLOGY

The kidneys receive 20% of the cardiac output. They are the main organs which maintain the internal environment through the processes of:

i. Excretion
ii. Conservation
iii. Regulation
iv. Hormonal functions.

The kidneys are the organs that receive the highest blood flow in the body at the rate of 4 mL/g of renal tissue. The metabolic activity of the tubular cells and their oxygen demand are high. The high

blood flow rate, high oxygen demand of the tubular cells, filtration of the plasma and metabolism of drugs and toxins in the kidney make this organ highly vulnerable to ischemic and toxic insults. Kidneys cannot withstand anoxia for long.

Excretion

The excess water derived by ingestion and metabolism is eliminated by the kidneys and skin. Urea formed by metabolism of dietary proteins, creatinine formed by catabolism of endogenous proteins and uric acid formed by metabolism of nucleic acids are eliminated mainly by the kidneys. In addition, the kidneys eliminate many other waste products and several drugs. The kidneys perform these functions by glomerular filtration, selective tubular reabsorption of essential substances and tubular secretion of waste products.

Conservation

Approximately 120 mL of fluid with several constitutents of normal plasma like electrolytes, glucose, amino acids and waste products are filtered every minute by the glomeruli. The tubules selectively reabsorb most of those substances which are essential for body, such as water, proteins, electrolytes, amino acids, glucose and the like. Most of the waste products like urea, creatinine, and uric acid which are not readily reabsorbed, remain in the tubular fluid to be excreted in urine. Some waste products are secreted into the urine. For example, H^+ ions, uric acid and drugs. Since nearly 99% of the water is reabsorbed by the tubules, the concentration of the substances may be even up to 100 times in the tubular fluid and urine, compared to their plasma levels. The calculation of urine to plasma (U/P) ratios of substances is used in order to assess the functional integrity of the tubules.

Regulation

The process of evolution from the unicellular organism in the sea to the most developed forms inhabiting land has taken more than 500 million years. Cellular metabolism will be deranged if gross changes in the composition of the extra-cellular fluid occur and therefore these have to be maintained within narrow ranges to preserve health and life. Water content of the body, sodium, potassium, other electrolytes and acid-base balance are regulated by the kidneys depending on the body's needs. When water intake is restricted, the kidneys compensate by reabsorbing more water from the tubules resulting in the formation of smaller quantity of concentrated urine. The reverse happens when fluid intake is excessive. A healthy adult should produce at least 400 mL urine in 24 hours to eliminate the metabolic wastes. This is the *obligatory urine volume.*

Urine output below 400 mL in 24 hours is termed *oliguria*. When the intake of water is excessive, more dilute urine is formed. Normal kidneys can eliminate up to 10 liters of water in 24 hours. Under normal circumstances, the fluid intake seldom exceeds 3 liters and it is easily excreted. Urine volume in excess of 3 liters in 24 hours is termed *polyuria*. Normal kidneys can conserve or eliminate salt within wide ranges and in health the urinary specific gravity can range from 1002 to 1030, which corresponds to osmolality ranging from 50 to 1200 milli osmols/kg (mOsm/kg). Nonvolatile acids produced in the system from diet by metabolic processes contribute to H^+ ion load at the rate of 1 mEq/kg body weight in 24 hours. Since the vegetarian diet contains less of H^+ ions and more of alkaline elements, the H^+ ion load for excretion in vegetarians is less compared to nonvegetarians. The H^+ ions are buffered by bicarbonate and other buffer systems and are eliminated by the renal tubules as titrable acid and ammonia. Thus, the kidneys help to maintain the pH of blood.

In health, the acid-base balance of the body depends on the coordinated function of the kidneys and the lungs. The lungs are capable of eliminating volatile acids like carbonic acid.

Hormonal Functions

The kidneys also function as endocrine organs. These processes include:

a. Production of erythropoietin for the regulation of erythropoiesis and possibly other functions.
b. Conversion of 25 dihydroxycholecalciferol into the metabolically active product I, 25-dihydroxycholecalciferol, which is concerned with the metabolism of calcium, phosphorus and bones.
c. Production of renin involved in the regulation of renal circulation and maintenance of blood pressure.

d. Prostaglandins maintaining autoregulation of renal circulation.
e. Bradykinin—A vasodilatory substance involved in renal autoregulation.

These functions are deranged in various renal diseases and accounts for many of the clinical features.

GENERAL PATTERNS OF MEDICAL DISORDERS AFFECTING THE KIDNEYS AND URINARY TRACT IN INDIA

Children

Renal disorders in children are mainly related to congenital or developmental anomalies such as phimosis, posterior urethral valve, abnormalities of ureter and bladder, incompetence of ureterovesical junction, and agenesis or hypoplasia of the kidney. Solid tumors like nephroblastoma are encountered more in children. Congenital or acquired abnormalities of the urinary tract predispose to urinary tract infection during infancy and childhood. If left untreated, these may lead to chronic renal failure with stunting of growth and skeletal deformities due to renal osteodystrophy in later life. Stone disease is also not uncommon in children. Post streptococcal glomerulonephritis is encountered more frequently, especially in the lower socioeconomic strata. Nephrotic syndrome is not uncommon. In older children, hypertension, unexplained pallor, bone deformities, nocturia or enuresis should make the clinician suspect a disorder of the kidneys and urinary system.

Young Adults

The most common disorder in this age group is glomerulonephritis presenting with proteinuria, hypertension, microscopic hematuria and varying degrees of renal failure. IgA nephropathy is now being recognized as the most common glomerular disease in young adults. Reflux nephropathy may also present with renal failure. *Hematuria* occurring in young and middle aged adults is generally due to glomerulonephritis, urinary calculi, urinary infection, surgical conditions such as new growths and ulcerations, and rarely hamorrhagic disorders. In women, the sexually active age group urinary infection is very common. Recurrent and persistent urinary infection is a common cause of chronic renal failure in later life. In addition to infection, pregnancy may be associated with pre-eclampsia accompanied by proteinuria, hypertension and renal dysfunction. Connective tissue disorders such as systemic lupus erythematosus and progressive systemic sclerosis also lead to renal problems in this age group.

Adults

Renal failure, both acute and chronic may occur at this period and it is usually the result of glomerulonephritis, interstitial nephritis acute tubular necrosis, obstructive nephropathy, urinary infection or inherited conditions such as polycystic kidney disease and Alport's syndrome. Several other systemic disorders which affect kidneys manifest with renal complications above the age of 40 years. These include diabetic nephropathy, hypertensive renal disease, ischemic nephropathy, drug induced nephropathy, tumors, nephrolitiasis, obstructive nephropathy and persistant infection. Polycystic kidneys may present as systemic hypertension, hematuria, chronic renal failure or abdominal masses.

Elderly Subjects

The most common problem is obstructive uropathy caused by enlargement of the prostate in men and prolapse of the genital tract in women. Chronic renal failure, persistent urinary infection and tumors contribute to the majority of problems in this age group. Elderly subjects whose renal function is subnormal are very susceptible to toxicity from drugs which are eliminated by the kidneys, e.g. aminoglycosides or radiocontrast agents.

The speciality of nephrology has reached a high level of development in India with several nephrology units, offering dialysis services and renal transplantation.

CHAPTER

29 Clinical Examination in Renal Diseases

R Kasi Visweswaran

General approach, Symptoms, Physical examination

GENERAL APPROACH

Several pathological processes may affect the kidneys, but the clinical manifestations take the form of only a limited number of distinct syndromes. As in the case of all other systems, a proper history, physical examination and basic investigations will help to arrive at an anatomic, functional and etiologic diagnosis and categorize the patient into one of the ten common syndromes in nephrology.

As the first step, the doctor should be able to identify a problem as of renal origin. The next step is to define the problem more specifically so as to narrow down the possibilities. For example, the symptom of hematuria may be further qualified as painful or painless. Painful hematuria occurring towards the end of micturition, with the presence of clots, may probably suggest a bladder stone, whereas recurrent bouts of painless hematuria may be a symptom of glomerular diseases like IgA nephropathy. Once the symptom is identified, the next step is to fit the condition into one of the classical syndromes such *as acute renal failure, chronic renal failure, nephrotic syndrome, acute glomerulonephritis, urinary infection, obstructions, stone disease, hypertension, tubular diseases and asymptomatic urinary anomalies*. The exact etiology and pathology can now be determined with the help of specific investigations.

SYMPTOMS

A patient with disease of the urinary system may fall into one of four categories:

1. Clear cut symptoms of involvement of the kidneys, ureters, bladder or urethra, e.g. edema, hematuria, oliguria, colicky pain, dysuria and others.
2. Systemic symptoms of renal insufficiency and uremia.
3. Symptoms of systemic diseases which lead to renal involvement, e.g. diabetes mellitus, collagen vascular disease, chronic sepsis, malignancy and others.
4. No symptom referable to excretory organs, but their pathology is detected incidentally in the course of a routine medical examination for other diseases or of an apparently healthy person, e.g. persistent proteinuria, elevation of blood urea or presence of abnormalities in ultrasonography.

A. *Symptoms referable to the kidneys include:*
 a. Facial puffiness and edema
 b. Alteration in the urinary output—oliguria or polyuria
 c. Alterations in the color and transparency of urine
 d. Hematuria
 e. Abdominal mass
 f. Fever with chills
 g. Pain in the lower abdomen
 h. Hypertension and its complications
 i. Symptoms of renal failure—acute or chronic renal failure and uremia.

B. *Symptoms referable to the ureters:* Ureteric colic, hematuria, abrupt cessation of urine flow, reflex anuria.

C. *Symptoms referable to the bladder, prostate and urethra:*
 a. *Pain:* Which can be identified as bladder pain, prostatic pain, or urethral pain
 b. *Other lower urinary symptoms:* Dysuria, frequency and urgency of micturition, abnormalities of the act of micturition such as obstruction or incontinence, abnormalities in urine such as hematuria, pyuria, calcuria and pneumaturia (gas bubbles in urine).

Facial Puffiness and Edema

'Puffiness of the face', more accurately described as periorbital puffiness of upper and lower eyelids bilaterally associated with swelling of the face as a whole (Fig. 29.1). In acute nephritic syndrome, it is more pronounced on waking up from sleep and of abrupt onset. In nephrotic syndrome, puffiness of face on waking up and ankle swelling towards the evening are of relatively insidious onset. The edema is often due to hypoalbuminemia with salt and water retension. It is more prominent in the dependent parts and in loose areolar tissue. The severity ranges from moderate to massive and associated with gross ascites, abdominal wall edema (Fig. 29.2) and genital edema. In chronic renal failure, the cause of edema may be either renal insufficiency, or cardiac failure secondary to hypertension. To elicit pitting edema, firm pressure is applied with the thumb over or below and behind the medial malleolus pressing against the underlying tarsal bone. After about 30 seconds when the thumb is removed, a depression will be seen in the skin which will fill up within the next 30 to 60 seconds. This is early pitting edema (Figs 29.3 A and B).



Fig. 29.1: Mild facial puffness



Fig. 29.2: Gross ascites with abdominal wall edema in nephritic syndrome



Figs 29.3A and B: Eliciting pitting pedal edema by pressing with thumb against medial malleolus

Alterations in the Urinary Output

The total quantity of urine in 24 hours should be collected properly and measured. In order to collect 24 hours sample from say 8 am to 8 am the next day, it is necessary to ask the patient to empty the bladder at 8 am on the first day and collect all the urine thereafter and including the urine passed at 8 am the next day. For any timed urine collection, it is necessary to remember that the collection time starts when the bladder is emptied and ends by collecting the sample at the specified time. Normal urine output ranges between 700 and 2500 ml in 24 hours and depends on the fluid intake, physical activity and atmospheric conditions such as temperature and humidity.

i. *Anuria:* When the output is less than 50 ml in 24 hours.
ii. *Oliguria:* When the output is less than 400 ml in 24 hours.
iii. *Polyuria:* When the output is more than 3000 ml in 24 hours.

It is important to note that normal urine output does not necessarily indicate that the kidneys are functioning normally. For example, in the early stages of chronic renal failure and nephrotic syndrome, the urine output may be within the normal range.

Anuria

All pathological conditions which cause oliguria can progress to anuria. However, if the anuria is absolute, i.e. the patient fails to produce even a drop of urine in 24 hours, the most likely possibility is total obstruction of the urinary tract and this has to be confirmed or ruled out by further studies. If the obstruction is distal to the urinary bladder, the distended bladder can be made out as a diffuse suprapubic swelling, which is dull to percussion. If the bladder is empty, the obstruction may be higher up, either in the ureters or renal pelvis. Unilateral sudden obstruction of the renal pelvis or ureter can lead on to reflex shut down of the other side leading to reflect anuria. Usually it is caused by massive clot, calculus or a necrosed renal pyramid. Absolute anuria may also occur in bilateral ureteric obstruction as seen in carcinoma cervix or when obstruction to ureter of a single functioning kidney occurs.

Oliguria

Oliguria may be due to prerenal causes, primary renal disease or other systemic diseases. Prerenal causes include conditions like reduction of fluid intake, transient hypotension and use of drugs with fluid retaining tendancy. It may be associated with loss of fluid from the body due to excessive sweating, gastroenteritis, hemorrhage, early stages of shock or due to sequestration of fluid within the body as in peritonitis, or crush injury. Renal causes include acute glomerulonephritis, acute tubular necrosis, renal cortical necrosis, nephrotic syndrome and others. Systemic diseases such as congestive cardiac failure, cirrhosis liver and hypoproteinemia are associated with intravascular volume contraction and present with oliguria even though the kidneys are normal.

Polyuria

Physiological polyuria occurs as a result of excessive intake of fluid as in hysterical or compulsive water drinking (psychogenic polydipsia) and normal fluid intake when the environmental temperature is low. Pathologically polyuria is often associated with conditions like diabetes mellitus, diabetes insipidus, diuretic phase of acute glomerulonephritis and acute renal failure, during treatment of all edematous conditions and after relief of urinary obstruction, i.e. postobstructive diuresis. Paradoxically, partial obstruction of the urinary tract may also produce polyuria since the back pressure resulting from the obstruction interferes with the tubular reabsorption of water and solutes. Use of several drugs may be associated with polyuria.

Changes in the Physical Characteristics of Urine

Normal urine is a straw-colored, odorless and clear fluid when freshly passed. The specific gravity ranges from 1002 to 1036 and is sterile when cultured. On standing it acquires the characteristic ammoniacal odor and may turn turbid. If freshly passed urine is foul smelling it suggests infection of the urinary tract.

Color of Urine

Concentrated urine is normally yellowish, owing to the presence of urochrome and uroerythrin pigments. On standing, it darkens due to the oxidation of urobilinogen to urobilin. Dilute urine is pale. In chronic renal failure the urine may be pale. In polyuric conditions such as diabetes mellitus, diabetes insipidus and during resolution of edema the urine is pale. The causes of abnormal color are given in Table 29.1.

Transparency

Even normal urine may become turbid on standing due to precipitation of urates and phosphates. Overgrowth of bacteria in urine samples collected and preserved for hours lead to opalescence of the urine. Sometimes even freshly passed urine may be turbid due to the presence of crystals *(crystalluria)*, pus *(pyuria)*, blood *(hematuria)*, necrotic material, or chyle *(chyluria)*. Although pyuria usually indicates infection of the urinary tract, but it may also occur in calculus disease, malignancies, medullary sponge kidney, renal

Table 29.1: Causes of abnormal color

Color	*Condition*
Red	Fresh blood
Reddish brown	Hemoglobin, myoglobin Drugs: rifampicin, pyridium, PAS, Congo red, desferrioxamine, methyldopa, L-dopa, niridazole, nitrofurantoin, metronidazole
Orange	Senna
Pink	Phenolphthalein and phenindione Porphyria-port wine color on standing Excessive ingestion of beet root
Yellow or brown	Bilirubin, urobilin, nitrofurantion homogentisic acid in alkaptonuria
Blackish	Melanin-occurring in metastatic melanomas
Blue or green	Methylene blue found in some proprietory pills, Indigo-carmine dyes, *Pseudomonas* infection

papillary necrosis or chronic noninfective tubulointerstitial nephritis. In chyluria the milkiness disappears on mixing the urine sample with chloroform since lipids are taken up by the chloroform layer. In acute glomerulonephritis the urine is smoky. This is caused by the presence of erythrocytes and the abnormal urinary sediments.

Hematuria

Presence of blood in urine is a common symptom in urinary disease. Hematuria may be macroscopic or microscopic. It may be painful or painless. Gross hematuria makes the color of urine red or brown. In less severe forms of hematuria urine appears to be smoky. In microscopic hematuria urine may appear to be normal. Under the microscope erythrocytes are seen as biconcave disks, singly or in clusters. At times they may be embedded in casts. When fresh urine is centrifuged, erythrocytes settle to the bottom, leaving the supernatant clear. However, the depth of color is not a totally reliable guide to the severity of blood loss, since even small quantity of blood in urine may give rise to alarming red color.

If a patient is made to pass urine under observation or is asked to collect separately the initial, middle and terminal streams of urine in 3 appropriately labeled containers, the hematuria can be classified according to the presence of blood in relation to the urinary stream. *Initial hematuria* occurs only at the beginning of micturition and the urine clears up as micturition proceeds. This occurs if bleeding is distal to the bladder. *Terminal hematuria* is usually caused by bleeding within the bladder and in posterior urethral lesions. In uniform hematuria, the urine is blood stained throughout and it indicates that the urine entering the bladder is already mixed with blood. This signifies renal or ureteric lesions.

Painful hematuria is associated with infections, stones, tumors and trauma. The hematuria that occurs with renal parenchymal diseases like glomerulonephritis, genitourinary tuberculosis and with some of the urothelial malignancies are generally painless. The presence of blood clots in the urine helps to rule out the possibility of glomerular disease. It has to be borne in mind that painless hematuria may become painful, if clots form and obstruct the lower urinary passages. Hematuria occurring in glomerulonephritis is usually associated with the presence of RBC casts in the urine. Since the casts are formed at the distal tubules, the red cells travelling through the tubules are entrapped into the cast and are passed in the urine as RBC casts. Hence, their presence in the urine is taken to indicate active glomerulonephritis. In hematuria the centrifuged urine sample will show sediment of red cells and clear supernatant.

The terms *hemoglobinuria* and *myoglobinuria* denote the presence of hemoglobin or myoglobin in urine. Since the pigments are free in the solution, the supernatant is colored in the centrifuged specimen. When large quantities of hemoglobin or myoglobin are released into the circulation as a result of intravascular hemolysis or crush injuries of muscles, these pigments appear in urine. Microscopy reveals no erythrocytes in hemoglobinuria and myoglobinuria but the chemical test for blood in urine will be positive. Special tests can be used to identify myoglobin.

Abdominal Swelling

Unilateral or bilateral swelling in the lumbar regions may be the presenting feature in cases of polycystic kidneys, renal neoplasms, hydronephrosis and pyonephrosis. Floating kidneys may be palpable in the iliac fossae as mobile masses. In thin individuals, the lower pole of the right kidney may be palpable even normally. During bimanual palpation, renal swellings are felt well with the hand in the loin.

Fever with Chills

Fever associated with chills and rigor is a common symptom of urinary tract infection. In the presence of structural lesions such as obstruction and calculi, the infection tends to become recurrent and persistent. Rapid onset of high fever exceeding 40°C accompanied by shaking chills and toxemia often suggests involvement of the renal parenchyma as in acute pyelonephritis.

This is associated with constitutional symptoms, nausea, vomiting and flank pain. Acute pyogenic infection of the prostate may also be associated with fever and chills.

Pain

Inflammation of the kidney leads to dull and constant pain felt in one or both loins. It is due to stretching of the renal capsule. *"Renal colic"* results from obstruction at the pelviureteric junction or the ureters. It is a severe colicky pain felt in the back between the twelfth rib and the iliac crest may last from a few minutes to several hours. It tends to radiate down to the groin or into the genitalia. Renal colic differs from the other forms of abdominal colic such as intestinal and biliary colic which usually manifest as recurrent bouts of intense pain lasting for brief periods. Renal colic is sustained and long-lasting, often punctuated by periodic excruciating pain.

Ureteric Colic

Pain resulting from obstruction and inflammation in the upper third of the ureter radiates to the testis of the same side. Obstruction in the middle third causes radiation of pain to the iliac fossa of the same side, and this may mimic the pain of appendicitis, if it is on the right side. The severe pain of renal colic makes the patient writhe about because no particular position of the body gives relief. This is in contrast to pain of acute appendicitis, where the patient lies quiet avoiding any movement, since movement aggravates the pain. Obstruction to the lower third of ureter causes pain radiating to the tip of the penis, scrotum or to the labia. Distal obstruction leads to proximal dilatation of the renal pelvis and ureters. If this is gradual, it may be painless. A constant dull pain may develop if infection supervenes as in pyonephrosis.

Pain Arising from the Urinary Bladder

Severe suprapubic pain felt especially towards the end of micturition suggests inflammation of the bladder (cystitis) or calculi in the bladder. In inflammation of the trigone and the posterior urethra, pain characteristically radiates to the tip of the penis. Pain due to inflammation of the prostate is localized to the perineum and may be aggravated during micturition. Urethral pain is often described as "burning" and may be associated with a constant painful urge to pass urine even though the bladder is empty. This symptom is called *strangury*. Strangury may occur if a stone is impacted or pressing on the trigone, acute trigonitis or pressure due to an overdistended bulb of a Foley's catheter. Constant urethral pain may suggest the presence of stone, tumor or foreign body inside the urethra.

Upward radiation of pain from the groin to the loin during micturition should suggest the presence of vesicoureteric reflux.

Other Lower Urinary Symptoms

The term "dysuria" refers to painful micturition. It is usually described as a "burning" or "stinging" sensation while passing urine. It is most commonly associated with lower urinary tract infections such as cystitis, prostatitis or urethritis. It may also be a symptom of bladder stones, tumor or foreign body.

Frequency of Micturition

Normal subjects pass urine about five times a day and that too only during waking hours. *In polyuria*, i.e. urine volume exceeds 3 liters in 24 hours, both frequency and the volume passed each time are increased. In inflammation of the bladder or urethra only the frequency is increased, not the volume of urine.

In anxiety state, enhanced parasympathetic activity leads to increased tone and irritability of the detrusor muscle, resulting in increased frequency of micturition even in the absence of local

disease. When the capacity of the bladder is reduced, frequency of micturition is increased.

Nocturia is the condition where the patient is woken up from sleep because of the urge to pass urine. In health 2/3 of the urine volume is formed during waking hours and only 1/3 during sleep. In several diseases states which give rise to diuresis, this pattern is changed and night urine may equal or exceed the day urine. *Nocturia* is common in diabetes mellitus, early stages of chronic renal failure, early stages of congestive cardiac failure and administration of long acting diuretic drugs, towards the latter half of the day. Need to pass urine while keeping awake at night need not be taken as nocturia.

Abnormalities of the Act of Micturition

The terms *urgency* and *precipitancy* refer to sudden uncontrollable urge to pass urine, with even passage of accumulated urine before reaching the toilet. The cause may be local or neurogenic. Common local causes include trigonitis, vesical stone, urethritis and prostatic enlargement. Neurological disorders leading to bilateral pyramidal tract lesions and dementia lead to urgency and incontinence.

Incontinence of urine is the inability to hold urine in the bladder. In most cases it results from lesion of the lumbosacral segments of the spinal cord and its distal connections. It may occur as a postoperative complication of prostatic surgery. In women, *vesicovaginal fistulae* may develop as a complication of obstructed labor and this leads to urinary incontinence.

In total incontinence, there is constant dribbling of urine through an incompetent or injured urethral sphincter or through fistulous communications. In overflow incontinence or false incontinence (also called *paradoxical incontinence)* or retention with overflow, the bladder fills and emptying is difficult due to mechanical obstruction to the urethra or bladder neck or failure of the urethral sphincter to open and start the micturition reflex. As the intravesical pressure rises it leads to intermittent dribbling of urine.

Stress incontinence is the involuntary passage of urine whenever the intra-abdominal pressure rises due to coughing, sneezing or laughing. This is more common in women. This may occur in prolapse of the uterus or other conditions causing laxity of the pelvic floor.

Enuresis is the term used to denote the involuntary voiding of urine during sleep. This is a normal phenomenon till the age of 2 to 3 years, by which time children develop complete control over the bladder and rectum. In 10% of normal children control over micturition is not full even after three years. In them also, voluntary control is achieved after varying periods of time. Causes of enuresis include psychological factors like anxiety and fear, organic lesions like urinary obstruction and infection and neurological disorders like spina bifida and paraplegias. Enuresis may be a symptom of polyuria.

The term *pneumaturia* indicates the presence of gas bubbles in the urine. Common causes include fistulous communications between the gut and the urinary tract and infection by gas forming organisms. It may also occur following instrumentation or surgery of the urinary tract.

Symptoms of Uremia

The retention of nitrogenous and other toxic waste products leads to the symptoms of uremia which is the result of advanced renal failure. Uremic symptoms are diverse, vague and nonspecific, referable to almost all systems of the body (Table 29.2).

Table 29.2: Symptomatology of uremia

General symptoms	Lethargy, mental confusion, loss of weight
Nervous system	Peripheral neuropathy, muscle cramps, myoclonus, epileptic seizures, coma
Cardiovascular system	Hypertension, pericarditis, arrhythmias, congestive heart failure
Respiratory system	Kussmaul's respiration, pleurisy, pneumonia, pulmonary edema
Skin and nail	Sallow pigmentation, pallor, dry and scaly skin, uremic frost over the face, pruritus, hyperkeratotic papules; half and half nail
Gastrointestinal system	Nausea, anorexia, vomiting, hematemesis due to gastric ulceration
Hematological	Anemia, hemorrhagic tendency
Metabolic and endocrine change	Osteomalacia, renal osteodystrophy, impotence, amenorrhea, complications during pregnancy

As a result, the uremic patient may present himself to different specialities initially.

Past History

History of acute glomerulonephritis, recurrent urinary infections, congenital abnormalities of the urinary tract, surgery on the urogenital tract, instrumentations including catheterization, and complications during pregnancy such as pre-eclampsia should be carefully elicited. In India, scabies with secondary bacterial skin infection is a frequent etiological factor for acute glomerulonephritis.

Drug History

Several drugs are capable of causing renal damage. Important among them are analgesics, non-steroidal anti-inflammatory drugs, aminoglycoside group of antibiotics, some of the recently introduced powerful antibacterial drugs, amphoterecin, radiocontrast agents, angiotensin converting enzyme inhibitors, cyclosporine, heavy metals, gold salts and many other agents. Improper dosing to children and elderly persons and those with compromised renal function is another important cause of drug related renal dysfunction. Many drugs and agents used in other systems of medicine are also toxic to the kidneys, Therefore, the history should reveal drugs taken by the patient in the recent and remote past, including their dose and duration.

Occupational exposure to several chemicals may lead on to renal tubular damage.

Family history is important since several renal disorders are hereditary with a strong genetic predisposition, e.g. *polycystic kidney, Alport's syndrome* and others. In autosomal dominant polycystic kidney disease, there may be other members in the family with identical problems. A careful family history for abdominal swelling, hematuria, hypertension, cerebrovascular accidents, or cysts in other family members help to strengthen the diagnosis and also detect the disease in asymptomatic relatives. In the case of Alport's syndrome, history of deafness or myopia due to keratoconus in other family members must be looked for.

Several familial diseases like diabetes mellitus, hypertension, collagen vascular disorders, and tuberculosis affect the kidneys. These have to be specially enquired into.

PHYSICAL EXAMINATION

Points in the general examination: Look particularly for edema, pallor, pigmentation and stigmata of uremia. Among the vital signs, general level of consciousness, rate and type of respiration and blood pressure are important. In any hypertensive individual, the blood pressure in all the four limbs must be measured at least once so that occlusive arterial disease as a cause of renal failure is not missed. Inspection of the abdomen, palpation of the kidneys and bladder, and examination of the genitalia are described in the Chapter 6.

CHAPTER

30 Investigations in Nephrology

R Kasi Visweswaran

Urine examination, Hemogram, Biochemical tests in blood, Radiology, Ultrasonography, Computed tomography scan, Endoscopy and catheterization, Histopathological studies, Isotopic studies, Appendix-1

URINE EXAMINATION

Volume

For measuring 24 hours urine volume, the patient should be instructed to void and empty the bladder and discard the urine at a specified time say, 8 am. The collection time starts now. All the urine passed subsequently, up to and including 8 am, the next day is collected in a bottle containing a preservative, usually 10 mL of glacial acetic acid. This is the 24 hours, urine specimen. If the time of collection of each specimen and its volume are charted, it helps to determine the volume of urine passed during day and night. Normal adult passes 700 to 2500 mL of urine in 24 hours.

If the 24 hours urine is to be collected for special tests or estimation of 17-ketosteroids, VMA or other metabolites, a large container with an appropriate preservative has to be supplied.

Specific Gravity

This is measured using a urinometer. The specific gravity depends upon the concentration of solutes present in the urine. Crystalloids like urea, salts and sugars raise specific gravity (SPGR) considerably, whereas colloids like proteins do so to a lesser extent.

Method

The urine is allowed to cool down to room temperature, since the urinometer is calibrated to be used at 16 to 20°C. The urinometer is suspended in the urine so that if floats, freely and the reading is noted without parallax error. If the room temperature is higher than that at which the instrument is calibrated, the actual SPGR is obtained by adding 0.001 for every 3°C increase above 20°C.

Normal SPGR ranges from 1002 to 1035. Urine passed in the morning is maximally concentrated in the majority of normal persons. Any SPGR above 1018, in the absence of abnormal constituents like glucose is evidence that the renal concentrating power is normal. When excess of liquids are consumed, the SPGR comes down to as low as 1003.

The SPGR can also be estimated by using a refractometer. The refractometer is calibrated for reading the refractive index and specific gravity of urine directly. Light rays falling on a prism are refracted by the intervening test fluid and the extent of refraction can be read from the meter. Only one drop of urine is needed for this estimation and it is based on the refractive index of solutions which varies with the SPGR (Fig. 30.1).

Osmolality

It is a more accurate parameter to express the concentration of solutes in urine. This can be measured using an osmometer it correlates roughly with the specific gravity (Table 30.1).

The osmolality of urine may vary from 50 to 1200 mOsm/kg water. The osmolality of plasma and the glomerular filtrate is about 285 mOsm/kg. In plasma the main substances which contribute to osmolality are sodium, glucose and urea and if



Fig. 30.1: Refractometer—The sample is placed in the oval glass of the refractometer and covered with the lid. The light rays pass through the prism under the oval glass disk and the refracted light is seen through the eyepiece. The scale as seen through the eyepiece is shown in the insert, which shows the scale of specific gravity or refractive index and the reading is at the junction of dark and light areas

Table 30.1: SPGR corresponding to different osmolality approximate

Specific gravity	*Osmolality (mOsm/Kg)*
1002	100
1010	285
1020	750
1030	1200
1035	1400

the concentration of these are determined, osmolality can be calculated by the formula:

Osmolality in mOsmol/kg = $2(Na^+$ mmol/L)

$$\frac{\text{urea mg/dL}}{6} + \frac{\text{glucose mg/dL}}{18}$$

Two examples are given below:

1. In a normal person with serum Na 140 mmol/L, serum, urea 30 mg/dL and glucose 90 mg/dL, the osmolality can be calculated as follows:

$$2(140) + \frac{30}{6} + \frac{90}{18} = 280 + 5 + 5 = 290 \text{ mOsm/kg}$$

2. In a diabetic with renal failure and the following blood chemistry, serum Na–140 mmol/L, urea-180 mg/dL and blood glucose 540 mg/dL. The plasma osmolality will be:

$$= (2 \times 140) + \frac{180}{6} + \frac{540}{18} = 280 + 30 + 30$$

$$= 340 \text{ mOsm/kg.}$$

Isosthenuria

In this condition, the urine SPGR remains constant around 1010 and the osmolality around 285 mOsm/kg. This results from the loss of concentrating and diluting functions of the renal tubules as is seen in chronic nephritis. 1010 is the SPGR of glomerular filtrate.

Urine Concentration and Dilution Tests

Normal persons should be able to concentrate the urine to SPGR 1018 after 8 to 12 hours of fluid deprivation. Failure to concentrate the urine to SPGR 1018 (mOsm 600–650) after overnight water deprivation, may indicate loss of ability to concentrate the urine and further investigations are required. This is done by continuing the water deprivation test with monitoring of pulse, blood pressure and body weight till 3% of the body weight is lost or postural tachycardia or hypotension occurs. In the normals, the urine SPGR rises above 1018. In conditions such as diabetes insipidus, even at this stage the urine SPGR does not rise above 1010.

After an intake of 1000 mL of water, a normal person should pass 750 mL of urine within 20 minutes and 1000 mL by 4 hours and at least one sample of urine collected half hourly should have SPGR below 1003.

Color

Normal urine is amber colored and clear (Fig. 30.2). The color may vary from light amber to yellow depending on the concentration of urine**.** Change in color may occur due to blood (Fig. 30.3), bile



Fig. 30.2: Normal urine



Fig 30.3: Hematuria

pigments, urobilinogen, prophobilinogen, other metabolites, pigments or several drugs. Turbidity of freshly voided urine may be due to pus, blood or crystals.

Smell

Fresh normal urine has no offensive odor. On standing it assumes an ammoniacal smell due to splitting of urea to ammonia by the bacteria. Fishy or offensive smell of fresh urine suggests urinary infection. Several substances like acetone, amino acids, methyl mercaptan in hepatic failure and aromatic substances derived from foods (e.g. garlic) may change the odor of freshly passed urine.

Reaction

Fresh urine is acidic in reaction with pH below 5.5. In vegetarians and those who take alkalies, the reaction may be mildly alkaline. The reaction is tested with litmus paper. The pH can be determined by a pH paper or pH meter. Pathologically, loss of the capacity of the tubules to eliminate acid leads to the production of alkaline urine. This happens in renal tubular acidosis. Urinary infection with *E. coli* makes the urine strongly acid. Infection by *B. proteus* makes the urine strongly alkaline. Uric acid stones occur in acid pH. Stones secondary to chronic infections develop in alkaline urine.

Therapeutic modification of urine pH is a common practice in the management of urinary infection. This gives symptomatic relief and also enhances the effectiveness of antibacterial drugs. In renal tubular acidosis urine pH is monitored in order to assess therapy.

Chemical Constituents of Urine

The main excretory products in urine are urea, uric acid, creatinine, several inorganic salts and organic substances. In addition, normal urine also contains minute amounts of proteins and glucose which are too low to be detected by the ordinary side room tests. When the amount of urinary albumin increases, but is still not detectable by the ordinary side room tests, it is called microalbuminuria and this denotes the presence of early stages of renal involvement, especially so in diabetic nephropathy. Screening for *microalbuminuria* is done in order to identify early stages of diabetic nephropathy. Appropriate management at this stage may prevent or delay the progression of diabetic nephropathy.

The routine laboratory tests include the detection of proteins, glucose, bile pigments and bile salts, acetone and microscopic examination of the centrifuged deposits. Under special circumstances several other substances passed in urine can be looked for e.g. urobilinogen, porphobilinogen, other sugars, amino acids, creatinine.

Tests for Proteins

Heat coagulation test detects all proteins in urine which include *albumin, Tamm-Horsfall protein, beta 2 microglobulin, immunoglobulins and other proteins:* "Albustix" detects only albumin. It is necessary to differentiate between albumin and other proteins in urine.

Heat coagulation and acetic acid test: A 15 cm long test tube is filled 2/3 with urine and the top of the column is heated to boiling over a flame, holding the test tube at its bottom. An opalescence develops if proteins or phosphates are present. At that stage two to three drops of 2% acetic acid is added through the side of the test tube. Opacity due to coagulated proteins persists whereas the one caused by phosphates disappears promptly. The density of opacity is generally proportional to the amount of protein in the urine. Normal urine does not give a positive heat test.

Dipstix test: *Dipstix* filter paper strips impregnated with chemicals and enzymes which change color when exposed to protein and *detects* the presence all proteins except light chains of immunoglobulins. "Albustix" strips are specific for albumin. The intensity of color gives an approximate idea of the quantity of albumin present and amount of albumin can be read off by comparison with standards.

Several other methods are available for side room detection of urinary protein.

Detection of Specific Proteins, Microalbumin and Amino acids in Urine

This can be done by electrophoresis, immunoelectrophoresis, chromatography and radioimmunoassay. These have to be performed in specialized laboratories.

The term *microalbuminuria* is used when the urinary loss of albumin ranges from 20 to 200 mcg per minute or 30 to 300 mg of albumin/day. This

can be detected only by tests like radioimmunoassay. Microalbuminuria can be diagnosed from a single random urine sample by estimating the albumin/ creatinine ratio. Before checking for microalbuminuria, regular urine test is done to rule out gross proteinuria and urinary tract infection. Patient should not be having fever and undertake unaccustomed physical activity. In those with diabetes and hypertension, the blood sugar and BP should be well controlled before undertaking the test.

Bence-Jones protein: This consists of the light chains of abnormal proteins secreted by neoplastic plasma cells in multiple myeloma and other plasma cell dyscrasias. These can be detected by a simple heat test.

Around 10 mL urine is taken in a test tube, acidified with 1 drop of 2% acetic acid, and heated in a waterbath. Bence-Jones protein precipitates as a cloud at 50°C. On continuing heating above 80°C it dissolves. This sequence is reversed on cooling the urine gradually.

Another sensitive test is to mix 5 parts of urine with 1 part of 5% acetic acid and 3 parts of saturated solution of sodium chloride. Proteins are precipitated at once. On boiling, Bence-Jones protein dissolves, whereas other proteins do not *When heat test is positive and dipstix test is negative, suspect Bence-Jones proteinuria.*

The time honored test for quantitative estimation is 24 hours urine protein: In conditions like nephrotic syndrome and other types of glomerular diseases the total protein lost in urine in 24 hours may correlate with the severity and response to treatment.

The biuret method is employed for quantitative estimation of proteins in urine. *In nephrotic syndrome the urinary protein* excretion exceeds 3.5 g/day or 2.0 g/m^2/24 hours.

Sugars

Detection of sugar is by boiling urine with copper-containing Fehling's reagent or Benedict's reagent which is reduced by glucose and the blue color progressively changes to green, yellow, orange and red depending upon the amount of glucose.

Eight drops of urine (0.5 mL) are added to 5 mL of Benedict's reagent and boiled for 2 minutes, cooled and the color is noted. Sugars reduce the copper and produce colors ranging from green to brick red, depending upon their concentration. This test is nonspecific since several substances like fructose, lactose, galactose, aspirin, vitamin C, and many drugs may give a positive test. But in any person in whom the reducing sugar has been identified as glucose, this simple test can be performed at home to monitor glycosuria.

Specific test for glucose is the glucose oxidase test. Glucostix test strips are available commercially. These tests are based on specific enzyme-mediated reactions which can also be quantified. These test strips are reliable and easier to perform, but more expensive. Test strips are unaffected by the other sugars or drugs. In view of reliability and ease of the test, strip tests should be preferred.

Acetone

Acetone, acetoacetic acid and betahydroxybutyric acid appear in urine in diabetic ketoacidosis. Other causes of ketosis such as prolonged starvation and repeated vomiting lead to the presence of acetone in urine. Test strips, tablets or conventional tests may be employed.

Rothera's test 5 ml of urine taken in a test tube is saturated with ammonium sulfate. Two drops of freshly prepared sodium nitroprusside solution is added and mixed. Liquor ammonia is added along the sides of the test tube. At the junction of the urine with liquor ammonia, a violet ring develops. The speed of formation of this ring and its intensity can be recorded. They correlate with the amount of acetone present. Serial performance of this test helps to monitor progress of ketoacidosis with treatment. Acetone disappears on boiling the urine.

Bile

Normal urine does not contain the constituents of bile. Presence of bile pigments and bile salts in urine reflect the rise in levels of conjugated bile pigments (which are water-soluble) and bile salts in blood. These abnormalities occur in obstructive jaundice.

Tests for bile pigments: Presence of bile pigments in urine is suspected by observing for yellow color of the froth over the urine held in a clean container.

1. To 5 mL of urine taken in a test tube, add 2 drops of tincture of iodine. Development of green color suggests the presence of bile pigments. This test is easy to perform, but nonspecific.
2. A more reliable test is to perform Fouchet's test. Around 5 mL of urine is boiled for 30 seconds with 2 mL of barium chloride solution. The precipitate is filtered through a filter paper and a drop of Fouchet's reagent is dropped on to the precipitate. Development of green or violet color indicates the presence of bile pigment.
3. Bile salts reduce the surface tension of urine. This is detected by gently dropping flowers of sulfur on to the surface of 15 mL urine taken in a test tube and kept still. In the presence of bile salts the particles of sulfur promptly sink to the bottom of the test tube. In normal urine, they float.
4. Test strips for detection of bile pigments are also available.

Urobilinogen

This is the urinary end product of bile pigment metabolism. Bile pigment which enters the intestines is converted into urobilinogen by bacterial action and part of it is reabsorbed by the enterohepatic circulation to reach the liver. Normal liver cells re-excrete most of this pigment into bile canaliculi, without allowing it to enter the systemic circulation, but a small part escapes into the systemic circulation, to be excreted by the kidney. This comes out as urobilinogen. The terms urobilinogen and stercobilinogen are used synonymously by different authors.

Around 2 mL of *Ehrlich's aldehyde reagent* is added to 5 mL of fresh urine. A pink color develops within 5 minutes. The depth of color and speed of its development depend upon the concentration of urobilinogen. If the color does not develop, gentle heating helps to accelerate the reaction.

Normal urine contains a trace of this pigment, which is detectable in the first morning urine. On diluting the urine to 10 times with water, and repeating the test urobilinogen is not detectable. If in spite of dilution urobilinogen test is positive, it indicates excess of urobilinogen.

Absence of urobilinogen indicates that bile pigment is not entering the intestines. This occurs in obstructive jaundice. Excess of urobilinogen in urine may be due to:

1. Release of excess of bile pigment into circulation as is occurring in accelerated destruction of hemoglobin in hemolytic anemia, or
2. Inability of liver cells to re-excrete stercobilinogen into bile, as is seen in hepatic parenchymal failure.

Porphobilinogen

This also gives positive test with Ehrlich's aldehyde reagent. To distinguish between urobilinogen and porphobilinogen, perform Ehrlich's test and add chloroform and mix by inverting the tube a few times gently. The color of urobilinogen is extracted by chloroform whereas the color of porphobilinogen is not.

Microscopic Examination of Urinary Deposits

Examination of urinary deposits gives diagnostic and prognostic clues in many of the renal diseases. This simple and inexpensive method must be mastered by all doctors. Urine microscopy may be considered the simplest alternative to renal biopsy since it gives reliable information about several structural lesions in the kidneys and urinary tract.

Method

Ten milliliter of freshly passed urine is centrifuged at low speed (1000 rpm) for 5 minutes. Hand centrifuge or an electric centrifuge may be used. Very high speed should be avoided since the casts may be distorted. A 9 mL of the supernatant is removed and the sediments are resuspended in the remaining volume by gentle shaking. A drop is taken on a glass slide, covered with a cover slip and examined under low power of the microscope. Further details of the deposits can be obtained by using the high power objective of the microscope (Figs 30.4 to 30.12). The WBC counting chamber can be used to count the various elements in the urinary sediment.

Normal urine may show a few erythrocytes, leukocytes, epithelial cells (Fig. 30.4) and an occasional hyaline cast. Presence of these elements in excess or other types of casts is abnormal. The daily excretion of these cells and casts in urine can be determined by doing *Addis count which is rarely done now a days.*

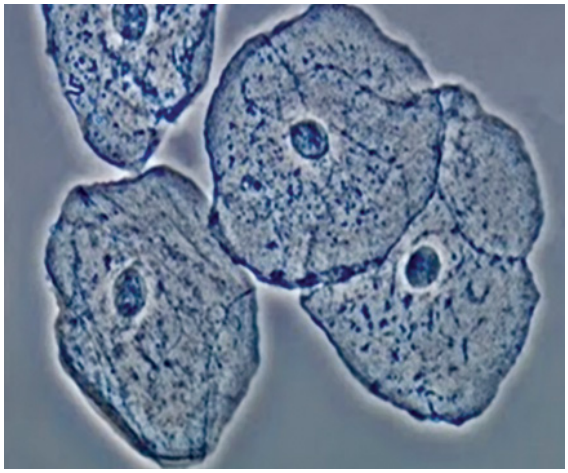


Fig. 30.4: Epithelial cells in fresh urine

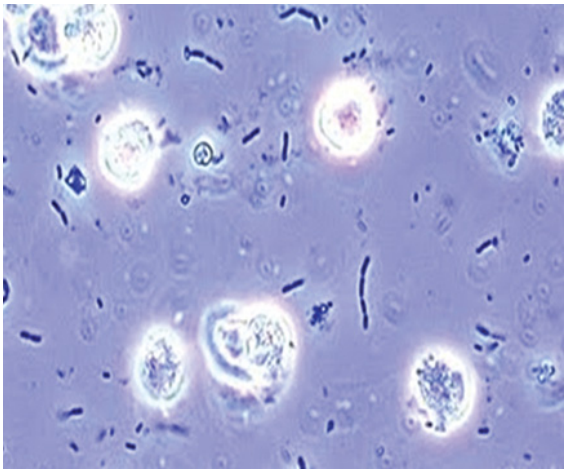


Fig. 30.6: WBCs and bacteria in fresh urine deposit

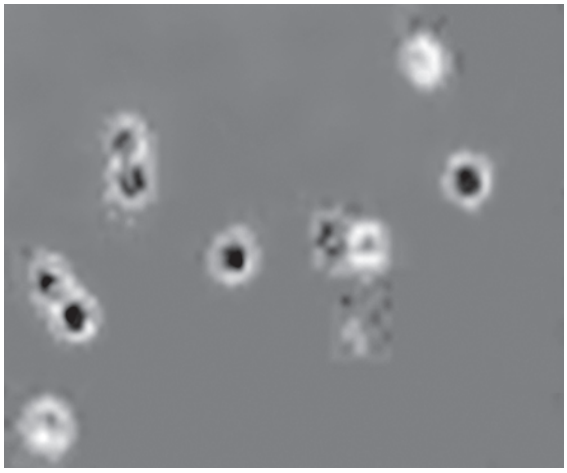


Fig. 30.5: RBCs in fresh urine seen as biconcave disk

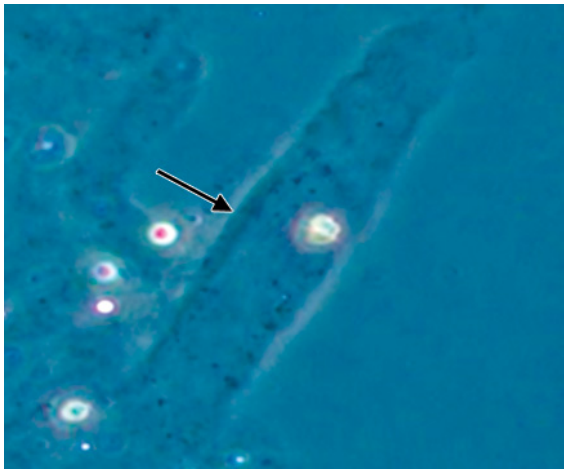


Fig. 30.7: Hyaline casts—fresh urine deposit

Approximate normal excretion rates are:

- Erythrocytes 30,000/hour
- Leukocytes 1,00,000/hour
- Renal tubular cells 68,000/hour

Presence of numerous erythrocytes in the deposit, without gross blood staining of urine constitutes microscopic hematuria (Fig. 30.5). This may occur in glomerulonephritis, tubular disease, infections, calculi, new growths, ulcerations and hemorrhagic disorders such as thrombocytopenic purpura.

Presence of pus cells in uncentrifuged urine suggests inflammation of the urinary tract such as acute and chronic pyelonephritis, cystitis and urethritis. Presence of bacteria in clean-catch fresh urine is suggestive of infection (Fig. 30.6).

Casts

Cast is cylindrical mould of the lumen of the distal tubule and collecting tubule and it is formed from coagulated *protein.* Hyaline casts are clear, homogenous and nearly transparent. It is formed mainly by Tamm-Horsfall mucoprotein which is secreted by the distal tubule (Fig. 30.7).

Other proteins and cellular elements get impregnated in the cast if they are present in the distal tubule at the time of it's formation. Casts can be differentiated into RBC casts, (Fig. 30.8) granular casts (Fig. 30.9) pus cell casts, tubular epithelial cell casts and leukocyte casts, based on the morphology. Presence of RBC casts suggests acute glomerulonephritis. In pyelonephritis, pus cell

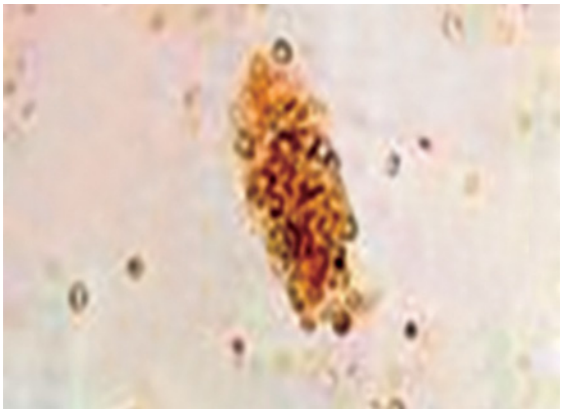


Fig. 30.8: RBC cast—urine deposit



Fig. 30.10: Uric acid crystals (mostly hexagonal)—urine deposit



Fig. 30.9: Granular cast—urine deposit

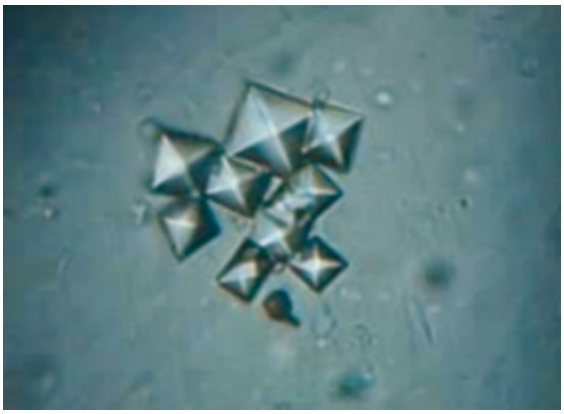


Fig. 30.11: Calcium oxalate crystals (envelop shaped crystals)—urine deposit

casts may be seen in plenty. Renal tubular epithelium may be seen on the casts in acute and chronic tubular lesions. Amyloid casts may be seen in renal amyloidosis only by special stains. Broad casts are characteristic of chronic renal failure since the distal tubules are dilated in this condition. When the cellular ingredients of the casts disintegrate, they take the appearance of coarse or fine granules in the cast leading to 'coarsely' or 'finely' granular casts. Preponderance of such granular casts suggests chronic parenchymal disease.

Various types of crystals, fat globules, and spermatozoa can be identified in the urine. The common types of crystals seen in urine deposits are triple phosphate, calcium phosphate, uric acid (Fig. 30.10), calcium carbonate, ammonium urate, tyrosine, calcium oxalate (Fig. 30.11), leucine, cystine, sodium urate, hippuric acid and cholesterol (Fig. 30.12). In endemic areas eggs of *Schistosoma hematobium* may be seen. Urine sediments may

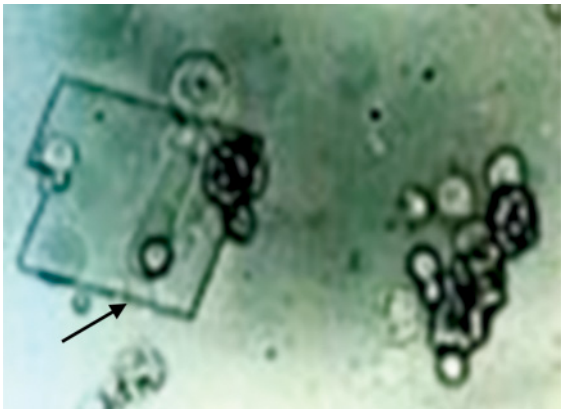


Fig. 30.12: Cholesterol crystals—urine deposit (arrow)

be subjected to special stains like methylene blue, Gram's stain or AFB staining to identify pathogenic bacteria or special stains for identifying malignant cells.

Bacteriological Tests

Clean-catch midstream urine samples are used for culture, isolation and identification of the organisms. In children and in adults where collection of clean-catch midstream sample is not possible, urine obtained by suprapubic aspiration of the bladder using a long needle connected to a hypodermic syringe may be used. As far as possible, urinary catheterization should be avoided, since chance of contamination is high.

Collection of Midstream Specimen of Urine

Midstream specimen of urine (MSU) can be collected from all types of patients who can understand the procedure and cooperate. Normally the urine collected by this method is sterile. This is the safest and simplest way to obtain urine for bacteriological culture.

Estimation of electrolytes, urea, creatinine, ammonia, citrate oxalate and uric acid concentrations in urine is done for confirming the diagnosis. Changes in urinary chemistry help to differentiate between pre-renal failure and established acute renal failure (Table 30.2).

HEMOGRAM

In chronic renal failure, anemia is an invariable accompaniment and is often normocytic normochromic anemia. The main reason is defective regeneration of erythrocytes due to lower levels of *erythropoietin*. This responds readily to exogenously administered erythropoietin. In patients on chronic hemodialysis and peritoneal dialysis programs, blood losses occur and iron deficiency develops which aggravate the anemia. Most patients also have associated iron deficiency and it should be corrected before instituting treatment with erythropoietin.

Renal tumors such as hypernephroma or inherited diseases like autosomal dominant polycystic kidney disease may be associated with *secondary polycythemia.* In all cases of apparent 'polycythemia vera' presence of renal abnormalities should be excluded by investigations.

Examination of a blood film may suggest renal failure, if the erythrocytes show abnormalities like *burr cells* which are erythrocytes with scalloped margins.

Neutrophil leukocytosis should suggest an infective lesion. Since immunosuppressive therapy is a major therapeutic modality in many types of renal disorders, monitoring the leukocyte and platelet count is an essential component of follow-up management. Platelet count may be reduced and platelet dysfunction may develop in uremic states.

Erythrocyte Sedimentation Rate

Very high erythrocyte sedimentation rate (ESR) often in excess of 100 mm/hour, should suggest lupus erythematosus, multiple myeloma or other immune mediated nephropathies. Abnormalities of coagulation may develop in uremic states. So also, abnormalities of hemostatic mechanism may lead to renal involvement as in hemolytic uremic syndrome and thrombotic thrombocytopenic purpura.

Table 30.2: Typical urine chemistry in prerenal cause of renal failure and acute tubular necrosis

Urine chemistry	*Pre-renal cause*	*Acute tubular necrosis*
Specific gravity	> 1018	< 1015
Urinary osmolality	> 500	< 300
U/P osmolality ratio	> 1.5	< 1.1
U/P urea ratio	> 8	< 3
Urinary sodium	< 10 mmol/L	> 40 mmol/L
Fractional sodium excretion (FPNa)	< 1	> 2
Renal failure index (RFI)	< 1	> 1

BIOCHEMICAL TESTS IN BLOOD

Urea is one of the end products of protein metabolism. Normal level of blood urea is 20 to 40 mg/ dL. Level of blood urea increases when glomerular filtration decreases as a result of impairment of renal function. Estimation of blood urea is a reliable, simple and almost universally available test for renal excretory function. Even in the absence of renal impairment, blood urea may be disproportionately high in dehydration, hypercatabolic states, prerenal azotemia and gross gastrointestinal bleeding. In pregnancy, the normal blood urea level is lower than in the nonpregnant states. It is low in hepatic

failure and inappropriate secretion of antidiuretic hormone. Some laboratories measure only the nitrogen content in urea molecule and express it as blood urea nitrogen (BUN). For all clinical purposes it is taken as 50% of the urea level. *Blood urea of* 60 *mg = BUN of 28 mg.*

For estimation of blood urea, venous blood is collected without anticoagulant or preservative and sent to the laboratory.

Serum Creatinine

Creatinine is an end product of endogenous muscle breakdown and since the rate of muscle catabolism remains steady in health, the levels of serum creatinine do not vary from day-to-day. (Normal 0.7–1.2 mg/dL). Creatinine is filtered completely by the glomeruli and is not significantly reabsorbed or secreted by the renal tubule. Unlike blood urea, its level is unaltered by the degree of hydration, protein intake and urine flow rate. Therefore, the level of serum creatinine remains steady over prolonged periods. Creatinine clearance is a reliable clinical parameter of glomerular filtration rate. Alteration in serum creatinine is a very reliable indicator of glomerular filtration rate.

Creatinine clearance: Normal creatinine clearance is 110 ± 15 mL/mt. This is obtained by performing the creatinine clearance test. In this test, the amount of creatinine in 24 hours urine is measured. Serum creatinine value is also determined during this 24 hours period. A simplified formula for calculating creatinine clearance is given below:

$$\text{Creatinine clearance (mL/mt)} = \frac{\text{Urinary creatinine (mg/day)} \times 5}{\text{Serum creatinine (mg/dL)} \times 72}$$

Creatinine clearance can also be calculated using the *Cockcroft and Gault formula,* from the age, body weight and serum creatinine value.

$$\text{Creatinine clearance (in mL/min)} = \frac{\text{140-Age in years} \times \text{Weight in kg}}{72 \times \text{Serum creatinine in mg/dL}}$$

The normal value is 15% less for females compared to males. Therefore, the result is multiplied by 0.85 for females. This formula is applicable for adults only.

In the same individual there is a fixed relationship between the serum creatinine level and creatinine clearance. Hence, it is not necessary to repeat creatinine clearance test for periodic short term follow-up. It can be assessed by serial monitoring of serum creatinine alone. When the serum creatinine doubles, the creatinine clearance is reduced by half, and so on.

Serum Uric Acid

Uric acid is an end product of purine metabolism and is excreted mainly by the kidneys. Hence the blood levels of uric acid may increase in proportion to the degree of renal failure:

Normal level:	Males	2.5-8 mg/dL
	Females	1.5-6 mg/dL

However, hyperuricemia may also occur in primary disorders of purine metabolism such as gout. Hyperuricemia by any cause can also lead to renal damage. The blood levels of urea, uric acid and creatinine are markedly lower in pregnancy. The rise of serum uric acid levels during pregnancy to the prepregnant level is suggestive of development of pre-eclampsia.

Serum Electrolytes

Normal serum sodium	(135-145 mEq/L)
Serum potassium	(3.5-4.5 mEq/L)
Serum bicarbonate	(22-27 mEq/L)

The serum sodium, potassium and bicarbonate have to be closely monitored in patients with acute renal failure (ARF), since timely correction of electrolyte imbalances and prevention of further deterioration are important in its successful management. In many cases the sodium and bicarbonate levels may be lower than normal. This may be due either to dehydration or dilutional hyponatremia. These must be differentiated before instituting therapy. Normal kidneys have a wide reserve to regulate and compensate for deficiency or excess of various electrolytes. In renal failure, this reserve capacity is grossly impaired. Fatal hyperkalemia may occur in patients with acute renal failure.

Therefore the serum potassium levels have to be closely monitored. If intake of sodium and potassium is within normal range, the kidneys maintain normal blood levels even if renal function is grossly impaired. But if the intake is increased or decreased, abnormalities of serum electrolyte levels develop. The body produces acid ions at the rate of 1 mEq/kg body weight daily. This is excreted

by the kidneys as titrable acid. When excretion is defective, the H^+ ions use up the bicarbonate reserve resulting in metabolic acidosis.

Calcium, Phosphorus, Magnesium

Normal Values:

- Calcium 8.8-10.2 mg/dL
- Phosphorus 2.5-4 mg/dL
- Magnesium 1.5-2.5 mg/dL

Estimation of these divalent ions is of importance in the management of chronic renal failure since their levels are altered considerably. In untreated chronic renal failure, there is hyperphosphatemia, hypocalcemia and hyperparathyroidism. Abnormalities of calcium and phosphorus develop in acute renal failure as well. But, being of shorter duration, their clinical impact is less, compared to that in chronic renal failure.

Serum Alkaline Phosphatase

Normal level is 1 to 13 KA units. The serum alkaline phosphatase levels correlate well with the extent of skeletal involvement and is useful in follow-up of patients with chronic renal failure.

Serum Acid Phosphatase

Normal level is 1 to 3 KA units. In metastatic carcinoma of the prostate, acid phosphatase level is increased. Prostatic tissue is rich in this enzyme. Digital examination or instrumentation of the anal canal and rectum may release this enzyme into circulation and lead to transient elevation of its level in blood for 24 to 48 hours. Therefore, samples for acid phosphatase should be drawn before such procedures are undertaken.

Serum Proteins

Serum albumin is considerably lowered in florid nephrotic syndrome. Alpha-2 globulins may be increased. When the proteinuria is nonselective, i.e. all the serum protein fractions are lost in urine in inverse proportion to their molecular weight, albumin and globulins may be reduced, e.g. nephrotic syndrome. In selective proteinuria where albumin is mainly lost, serum albumin level alone drops.

Lipids

Various lipid abnormalities are seen in renal diseases. Nephrotic syndrome and chronic renal failure are associated with characteristic lipid abnormalities such as elevation of serum cholesterol, triglycerides and alteration in the lipoprotein profile. Detection of these abnormalities helps in diagnosis. Since longstanding hyper-lipidemia accelerates atherosclerosis, proper intervention to normalize the lipid profile forms part of therapeutic management. However, in steroid responsive nephrotic syndrome, the lipid abnormalities correct themselves when the nephrotic syndrome remits.

Urine to Plasma Ratios (U/P Ratios)

Measurement of the ratio of the concentration of substances between urine and plasma is employed to assess functional defects in the nephron.

In an oliguric patient, measurement of these parameters will enable the clinician to decide whether the oliguria is due to prerenal causes or acute tubular necrosis. In a patient who has dehydration, hypotension and oliguria in the initial stages, the renal tubules avidly reabsorb the water and sodium. So, the osmolality is high, specific gravity is >1018, but urinary sodium is low. <10 mmol/L). The urine to plasma osmolality will be >1.5. The urine to plasma urea ratio will be >8.1. The oliguria is due to increased reabsorption of water from the tubules.

If the above patient has a more severe injury or prolonged damage, the renal tubules undergo necrosis. Then, the glomerular filtration is automatically reduced and the oliguria is the result of reduced GFR. Since the tubule is unable to reabsorb the filtered sodium, the urinary sodium will be higher. The damaged tubule cannot concentrate the urine, so the urinary osmolality is <300, urine specific gravity <1010, and urine to plasma urea ratio < 3.1. The urinary sodium will be >40 mmol/L. Urinary sodium will not be reliable if the patient has been given diuretics. There are two indices which can be calculated from the urine chemistry.

Fractional sodium excretion (FE–Na^+)

$$\frac{\text{Urinary sodium (mmol/L)}}{\text{Plasma sodium (mmoI/L)}} \times \frac{\text{Plasma creatinine (mg/dL)}}{\text{Urinary creatinine (mg/dL)}} \times 100$$

Renal failure index (RFI)

$$\frac{\text{Urinary sodium}}{\text{Urinary creatinine}} \times \text{Plasma creatinine} \times 100$$

Both indices will be below 1 in renal failure due to prerenal causes and above l in acute tubular necrosis.

Tests for Tubular Damage

Determination of the concentrating and diluting function of the kidney helps to assess tubular function. The *enzyme N-acetyl-B-glucosaminidase* (NAG) which is present in normal tubular cells is excreted in larger amounts in urine, in cases of tubular damage. A dipstix is available for detection of NAG.

Presence in urine of β_2 *microglobulin* and *retinol binding protein* (RBP) which are low molecular weight proteins, normally filtered, but largely reabsorbed and metabolized by the tubules, indicates damage of proximal tubules.

IMAGING OF THE URINARY TRACT

Radiology

Plain Radiograph of the Abdomen

Kidney, ureter, bladder, urethra (KUBU) film: Plain radiographs may be required as an emergency investigation to find out the cause of renal colic or frank hematuria. A properly taken KUBU should include the abdomen from eleventh thoracic vertebra to the lower margin of inferior pubic ramus including the soft tissue shadow of external genitalia and both flank lines of extraperitoneal fat. The lateral border of psoas muscle should be clearly visible (Fig. 30.13). Normal kidneys are seen clearly if the preparation for the X-ray and exposure are optimal. The kidneys should be of normal size and equal. Reduction in length of one kidney by more than 2 cm suggests abnormality. Presence of calculi in the urinary passages, soft tissue calcification especially in the renal parenchyma and arteries and abnormalities in the vertebrae and pelvic bones should be looked for.



Fig. 30.13: Normal KUB X-ray. In this film psoas shadow is seen on the left side. The position of the kidney are marked, inferior ramus of the pubis and external genitalia are not included. This is not a KUBU film

Intravenous Urogram

Intravenous urogram (IVU) is a useful test for assessing renal function as well as the anatomy of the urinary passages. Adequate renal function is a prerequisite for getting proper visualization of contrast. Prior bowel preparation is essential to get good pictures. In elective cases the patient is given activated charcoal to adsorb intestinal gases (2–3 tablets thrice a day) for 2 days preceding the test. On the night previous to the test a purgative, preferably castor oil 30 mL is given to clear the bowel. Fluid restriction for 12 hours is also advised. The radiocontrast agent is eliminated by glomerular filtration and tubular excretion. Better pictures are obtained if the concentration of the agent in urine is higher.

A plain radiograph is taken first and contrast is given IV after proper tests for hypersensitivity. The radio-opaque dye is generally the meglumine salt of iothalamate or diatrizoate which contain iodine. Nonionic contrast media are preferred now. Passage of the contrast agent though the renal cortex gives the image and outline of the kidneys called the nephrogram. Subsequently the calyces, pelvis, ureters and bladder are shown up.

X-rays are taken at 1 minute, 3 minute, 5 minute, 10 minute, 15 minute, 30 minutes and later, if found necessary. Once the bladder is visualized a post-micturition film is also taken to ascertain whether the bladder empties fully. A nonfunctioning kidney does not take up the dye and the nephrogram phase does not occur. In acute tubular necrosis, the dye is taken up by the renal parenchyma, but not excreted into the tubules, thereby resulting in progressive increase in the density of the nephrogram with non-appearance of pyelogram. When the urinary

tract is obstructed, the back pressure on the collecting system can be identified as proximal distention of the ureter, dilatation of the pelvis and clubbing of the calyces. Chronic pyelonephritis produces distortion of the pelvicalyceal system. Anatomical abnormalities such as double ureters, hydronephrosis, renal tumor, polycystic kidneys, tumors in the collecting system, stones and indentation in the bladder neck produced by enlarged prostate can be demonstrated shows a normal IVU (Fig. 30.14).

Complications of IVU include anaphylactic reaction following dye injection, convulsions, a "hot flush" and rarely renal failure following larger doses of the dye. These complications are less common with the low osmolar, nonionic contrast media. In multiple myeloma the risk of renal failure following administration of iodinated contrast media is high.

Modifications of intravenous urogram: These are done specifically to diagnose particular diseases. A *rapid sequence* IVU is done in cases of hypertension suspected to be caused by unilateral renal artery stenosis. There will be delay in the appearance of the contrast on the affected side at 1, 2, 3 or 4 minutes after the injection of the dye. The size of the kidney may be smaller. In later pictures the concentration of the dye may be more than that of the normal side.

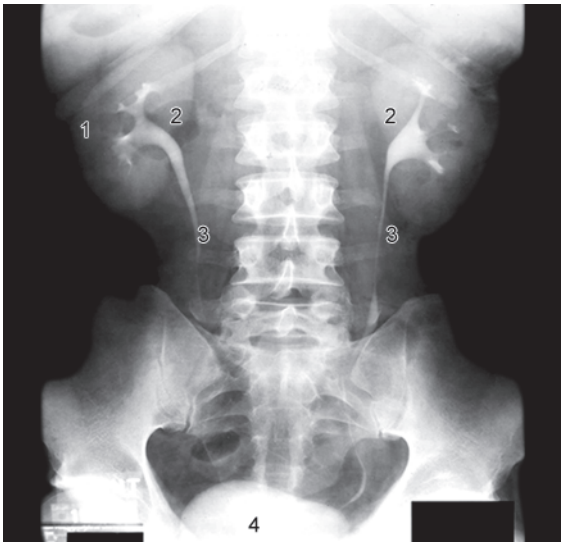


Fig. 30.14: Normal IVU. Showing nephrogram on both sides. The kidneys, renal pelvis, ureters and part of the bladder are visualized by the dye-numbered 1–4. The base of the bladder is not included in this film

High dose infusion pyelogram (double dose contrast IVU): It was employed previously to delineate the urinary system in patients with renal failure. This is not commonly done now due to risk of complications and the availability of other methods for diagnosis.

Retrograde pyelogram (RGP): The urinary passages are visualized by introducing contrast dye into the ureter by retrograde catheterization. Through a cystoscope, ureteric catheters are introduced and 4 to 6 mL of iodinated dye is injected into the ureter or renal pelvis and pictures are taken. This brings out the pelvicalyceal systems and ureters clearly.

Antegrade pyelogram (AGP): The radiocontrast dye is injected directly into the renal pelvis through percutaneous puncture or nephrostomy tube and X-rays are taken to visualize the level of obstruction in the ureter. Micturating cystourography (MCU) is show in Figure 30.15.

In this test, the bladder is catheterized and diluted contrast medium (40 mL of Conray 420 in 350 mL N. saline) is instilled to fill the bladder. The catheter is removed and patient is asked to void. Pictures are taken in the oblique position during the voiding phase. This helps to identify:

I. Reflux of urine from the bladder to one or both ureters.
II. To detect posterior urethral valve.
III. To detect abnormalities of the bladder neck and urethra.

ANGIOGRAPHY

Flush abdominal aortogram: This is done by injecting dye into the aorta above the renal arteries through a catheter introduced through the femoral or brachial artery. Films are exposed at the rate of one film per second for 5 to 6 seconds. This helps to study the aorta and its branches. Various abnormalities like position, number, branching pattern, occlusion, dilatation, stenosis of blood vessels and collateral circulation to organs can be identified. These studies are also sometimes necessary to visualize the vascular pattern of the kidneys of the donor for transplantation.

Selective renal arteriogram: A special arteriographic catheter is positioned in the renal artery and pictures are taken after dye injection, the arterial pattern of the kidney can be studied in detail.

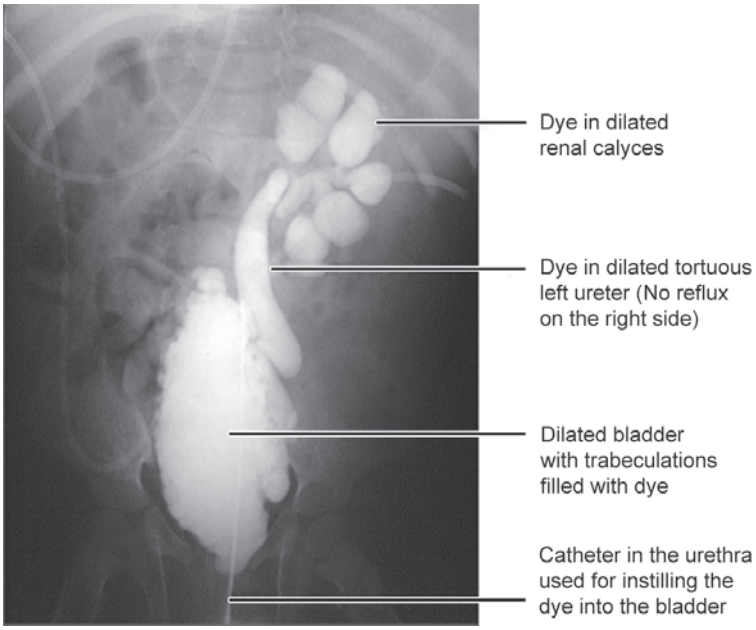


Fig. 30.15: Micturating cystourethrogram showing gross reflux of the dye instilled into the bladder proximally, even during the filling phase

In addition, dilatation of narrowed segments using balloon catheters *(percutaneous transluminal renal angioplasty)*, occlusion of vessels which feed tumors or vascular malformations by the injection of substances like gelfoam and other procedures can be undertaken by selective renal artery catheterization.

Digital subtraction angiogram (DSA): This gives an angiographic picture without interference from other structures such as bones, gas and soft tissues. Since the clarity is very good, intravenous DSA can be performed by giving a smaller volume of the dye into a peripheral vein as a bolus and taking the pictures as the bolus travels to the abdominal aorta and renal arteries.

Renal vein catheterization helps to obtain samples from either side and estimate renin and other substances.

ULTRASONOGRAPHY

As in the case of all other specialities ultrasonography has become a very elegant investigatory modality in the diagnosis of anatomical abnormalities of urinary system. The kidneys and adrenals can be clearly visualized. Their size, almost all morphological abnormalities like enlargement, contraction, distortion, tumors, cysts, abscesses, stones and other abnormalities can be clearly delineated. So also the ureters, urinary bladder and prostate can be visualized. Amount of residual urine in the bladder can be determined. Ultrasound aided procedures such as renal biopsy, and surgical operations are employed frequently. Doppler studies help to assess the blood flow and hemodynamics in the abdominal aorta and renal arteries and their branches. These studies are of great value in the assessment of several pathological states. Whenever facilities exist, ultrasound investigation should be done before undertaking any invasive procedure like IVU or retrograde catheterization.

COMPUTED TOMOGRAPHY SCAN

Computed tomography (TC) can reveal the size of the kidneys, morphological abnormalities, details of vasculature and presence of other abnormalities in the abdomen. It is helpful in the detection and staging of malignancies of the urinary tract great strides are being made in this technique. CT urogram, MR angio, spiral CT and MRI scan are the other recent diagnostic investigations.

ENDOSCOPY AND CATHETERIZATION STUDIES

The urethra can be visualized by urethroscopy and urinary bladder can be visualized by *cystoscopy.* Through the cystoscope therapeutic procedures such as removal of stones and biopsies of visible lesions can be done. Ureteric catheterization helps to collect urine from the two kidneys separately and to inject contrast medium into them. Estimation of the volume of urine from each kidney and tests performed on each sample helps to pinpoint the lesion to one side. Localized infection on one side can be established with certainty.

HISTOPATHOLOGICAL STUDIES

Percutaneous Renal Biopsy

Histological examination of the kidney is essential for proper diagnosis, assessment of renal damage, to institute appropriate therapy and to give a prognosis. Renal biopsy has come to stay as one of the most specific diagnostic methods in renal diseases. Since the clinical pattern may be similar in different renal disorders, histological diagnosis is of great value in establishing the pathology. For example, nephrotic syndrome may be caused by several conditions such as minimal change nephritis, diabetic nephropathy, renal amyloidosis and quartan malaria. Only renal biopsy may give conclusive result.

Biopsy can be done in the general medical wards by the internist, but preferably it should be undertaken in a nephrology unit. Biopsy is done with special biopsy gun. Automatic spring loaded biopsy guns are available which are more efficient and less traumatic. The kidney is approached from behind (see surface marking of kidney, for details). Ultrasound guided renal biopsy is more successful than blind biopsy in getting a proper specimen.

Indications for Renal Biopsy

1. Nephrotic syndrome except clear-cut minimal change nephritis occurring in children.
2. Unexplained renal failure with normal sized kidneys.
3. Diagnosis of renal involvement in systemic diseases, e.g. amyloidosis, sarcoidosis, drug toxicity, SLE.
4. Asymptomatic proteinuria or hematuria.
5. Failure to recover from apparently curable diseases (ARF).

Diagnosis of transplant rejection.

Contraindications for Percutaneous Renal Biopsy

1. Single kidney.
2. Horseshoe kidney or ectopic kidney.
3. Hemorrhagic disorders.
4. Severe hypertension.
5. Technical difficulties such as gross obesity, skeletal deformities, local sepsis and uncooperative patient. In small children, short anesthesia or supervised short acting sedative administration can be used for positioning the child and biopsy.

Procedure

The position of the kidney is confirmed by radiology and/or ultrasonography. The biopsy needle is introduced percutaneously after infiltrating local anesthetic 2% xylocaine. The patient holds his breath during the insertion of the needle into the kidney. The needle position can be inferred clinically by the movement of the needle corrosponding with respiration. Free movement of the needle should not be restrained at this time when the patient is breathing. The position of the tip can be confirmed by ultrasonography. A core of tissue is obtained for biopsy. The tissue is sent for histology and immunofluorescence studies. Microbiological studies and electron microscopy are requested for if necessary.

Following the biopsy a pressure dressing is applied over the biopsy site to minimize the hematoma. The patient should rest in bed for 24 hours and his fluid intake is increased to 3 L in 24 hours to induce diuresis and avoid clot colic if bleeding occurs. Pulse rate and blood pressure are monitored 2 hourly for 6 to 8 hours to detect bleeding.

Complications include bleeding, perirenal hematoma and infection. Microscopic hematuria

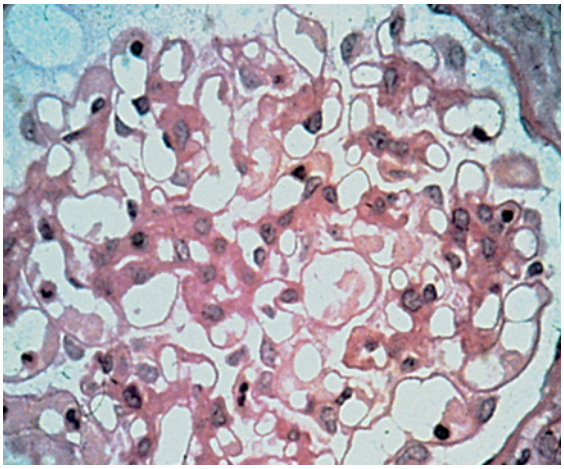


Fig. 30.16: H and E staining of normal glomerulus in light microscopy

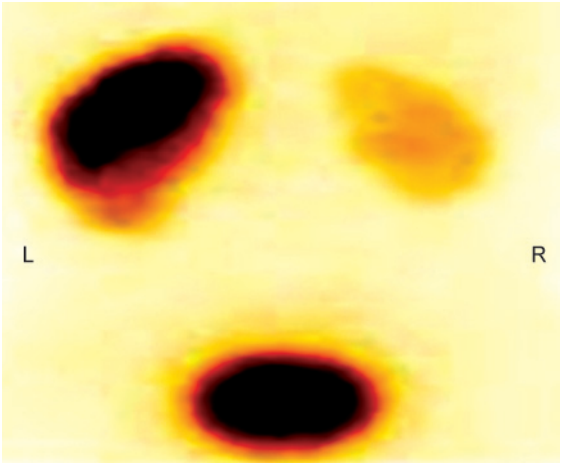


Fig. 30.17: Isotope renogram showing retention of DTPA in the collecting system of the left side. There is no retention on the right side. The bladder is full

occurs invariably and it is self-limiting. If more severe blood loss occurs resulting in hypotension, blood transfusion may be required. Very rarely surgical intervention may be needed.

Renal biopsy is an invasive procedure associated with a complication rate of 2 to 5% and a mortality rate of less than 0.1%. With the advent of ultrasound for marking or guiding biopsy and the use of the biopsy gun, the complication are reduced to very low levels in experienced hands.

Biopsy specimens are processed for histopathology, morphology by H and E stain, (Fig. 30.16) PAS stain, silver stain, trichome and others special stains. Frozen sections are used for immunofluoresence. Demonstration of immunoglobulin IgG, IgM, IgD, IgA, IgE, and complement components such as C_3 Clq and others can be done using fluorescein tagged appropriate antibody and fluorescence microscope. The quantitative and qualitative information so obtained helps to make specific diagnosis.

Another method to demonstrate immunoglobulins is by using immunoperoxidase staining methods.

ISOTOPIC STUDIES

Dynamic Renal Scintigraphy

The radiopharamaceutical most often used is ^{99m}Tc-DTPA (diethylene) triaminepenta-acetic acid) or ^{123}I labeled orthoiodohippuric acid (hippuran). The DTPA is excreted by glomerular filtration, whereas hippuran is both filtered and secreted by the tubules. Isotopic investigations are employed to study:

1. Renal blood flow
2. Obstructive uropathies (Fig. 30.17)
3. Bladder emptying
4. Glomerular filtration rate.

Static Renal Scintigraphy

This is done using ^{99m}Tc DMSA (dimercaptosucecinic acid) which is taken up by tubular cells, in proportion to renal function. The function of each kidney can be estimated separately using citrate labeled gallium or leukocytes labeled isotopically. Foci of infection in the urinary tract can also be identified accurately.

APPENDIX-1

SI Units (International System of Units)

SI units are used by the international scientific community. The use of a single system of measurement will improve the comparability of test results between countries. Many journals have adopted SI units. Quantitating a substance in moles (SI units) rather than in grams (traditional unit) allows an easier understanding of molecular relationships.

	Traditional unit	*Conversion factor*	*SI unit*
Urea nitrogen	8-18 mg/dL	0.357	3-6.5 mmol/L
Serum creatinine	0.6-1.2 mg/dL	88.4	50-110 micromol/L
Urinary creatinine Male	20-26 mg/kg/24 hrs	0.0088	0.18-0.23 mmol/kg/24 H
Urinary creatinine Female	14-22 mg/kg24/ hrs	0.0088	0.12-0.19 mmol/kg/24 H
Plasma glucose (fasting)	70-110 mg/dL	0.05551	3.9-6.1 mmol/L
Uric acid—serum	2-7 mg/dL	59.48	120-420 mcmol/L
Serum potassium	13.7-19.5 mg/dL	0.2558	3.5 - 4.988 mmol/L
Serum sodium	135-147 mEq/L	1	135-147 mmol/L
Serum phosphorus	2.5-5 mg/dL	0.3229	0.80-1.60 mmol/L
Serum calcium	8.8-10.3 mg/dL	0.250	2.20-2.58 mmol/dL
Serum bicarbonate expressed as CO_2 content	22-28 mEq/L	1	22-28 mmol/L

Note: Though the SI units were introduced with great enthusiasm, subsequently at least a few journals have gone back to the traditional units, they being more user-friendly.

SECTION

11

Neurology

CHAPTER

31 General Considerations in Neurology

AS Girija, KV Krishna Das

Arterial supply, Veins of the brain, Spinal cord, Meninges, Cerebrospinal fluid, Symptomatology in neurological disorders, Motor function, Sensory function, Profile of neurological disorders in India

INTRODUCTION

The nervous system is composed of two parts: the central nervous system (CNS) and the peripheral nervous system (PNS). The central nervous system is composed of the brain and the spinal cord. The peripheral nervous system consists of the cranial and spinal nerves. The autonomic nervous system (ANS) although functionally a separate system, is part central and part peripheral.

The human brain, weighing about 1400 g and constituting about 2% of the total body weight consists of neurons and their connections. It is developed from ectoderm. Most of the central nervous system develops in the first twelve weeks of embryogenesis. Infections in the mother or toxic causes lead to malformations of the nervous system, if they occur during this period. All information we have concerning our own body and the outside world is received centrally by the brain through the sensory pathways. The brain is concerned with all kinds of voluntary motor activity and regulation of visceral, endocrine and somatic functions. The brain is also concerned with such higher mental functions as consciousness, thought, memory, attention, emotion, creative and imaginative ability, speech and sleep.

The brain and the spinal cord are metabolically highly active organs in the body demanding about 17% of the total cardiac output and about 20% of the total oxygen consumption. The normal cerebral blood flow is about 750 mL per minute (i.e. 50 mL per 100 g of tissue). The mean oxygen consumption is about 3.3 mL 100 g of brain tissue per minute. Glucose is the metabolic fuel for the neurons. Both hypoxemia and hypoglycemia produce neurological dysfunction promptly. Disruption of arterial blood flow to the brain for more than five minutes may result in permanent damage to nerve cells. Hyperglycemia can also lead to neuronal dysfunction under pathological states.

ARTERIAL SUPPLY

The brain is supplied by the two internal carotid arteries (ICAs) and the two vertebral arteries (VAs). The ICA, after its origin at the bifurcation of the common carotid artery in the neck, passes up to enter the intracranial cavity through the carotid canal of the temporal bone at the base of the skull. The ICA can be divided into four segments-cervical, intrapetrosal, intracavernous and supraclinoid-the latter two segments form the "carotid siphon". In the cavernous sinus, it is in close relationship with the third, fourth, sixth and the first division of the fifth cranial nerves. The supraclinoid segment of ICA gives rise to all major branches-ophthalmic, posterior communicating and anterior choroidal arteries, and finally divides into anterior and middle cerebral arteries at the level of the optic chiasma.

The vertebral artery (VA) which arises from the first part of the subclavian artery, passes upwards through the foramina in the transverse processes of the upper six cervical vertebrae and

enters the posterior cranial fossa through the foramen magnum, after piercing the atlanto-occipital membrane and the dura mater. The two VAs on either side course upwards on the anterolateral surface of the medulla and unite with each other at the lower border of pons to form the basilar artery. The basilar artery ascends in a groove on the anterior surface of the pons and at its upper border, divides into the right and left posterior cerebral arteries.

Knowledge of the arterial supply to the brain (Table 31.1) is essential because cerebrovascular accidents caused by thromboembolic occlusions or hemorrhage occurring in specific arteries give rise to characteristic neurological deficits, e.g. carotid hemiplegia caused by occlusion of the trunk of the internal carotid artery, lateral medullary syndrome caused by occlusion of posterior inferior cerebellar artery and others. Cerebrovascular occlusion may result from arterial disease affecting the intracranial arteries, extracranial portions of these arteries, or from emboli arising from the heart as in valvular disease and ischemic heart disease.

VEINS OF THE BRAIN

The cerebral veins which have neither muscular tissue nor valves consist of two groups superficial and deep. Superficial veins drain the cortex and subcortical white matter and empty into the superior sagittal, cavernous, petrosal and transverse venous sinuses. The deep veins from the peri ventricular regions, diencephalon, basal ganglia and deep white matter drain into internal cerebral vein and great cerebral vein of Galen. These two groups of cerebral veins, interconnected through several anastomotic channels, pass through the subarachnoid space to empty into the venous sinuses which lie between the meningeal and periosteal layers of the dura mater.

Knowledge of the venous anatomy and physiology is essential to comprehend several disease mechanisms. Absence of valves in the venous system facilitates flow of blood in either direction in the major venous channels depending upon the level of intracranial, intrathoracic and intra-abdominal pressures. Egress of venous blood is a compensatory mechanism to lower intracranial pressure. Retrograde flow into intracranial veins makes the brain vulnerable to develop malignant metastases and abscess formation, secondary to lesions in the thoracic and abdominal cavities. Since venous flow in the large sinuses tends to be sluggish, cerebral venous thrombosis is a common complication of hypercoagulable states such as postpartum thrombosis, dehydration, polycythemia and others. Occlusion of venous drainage leads to rise in intracranial pressure. Thrombosis of the cavernous sinus is a dreaded complication of sepsis over the central portion of the face and nose. It leads to facial and orbital edema, paralysis of ocular nerves and a characteristic clinical picture. Due to intercommunication, affection of one side soon involves the opposite side too.

Though the vascular territories of the brain are anatomically distinct, considerable overlap and variations exist even in health. Moreover the blood flow in each territory is also determined by other factors such as arterial narrowing, presence of collaterals and others. Though syndromes of vascular occlusion generally run true to type, sometimes, the clinical effects may not truly correspond to the anatomical vascular supply.

Table 31.1: Arterial supply to the deeper areas in the brain, brainstem, and cerebellum

Corpus striatum and internal capsule	Medial and lateral striate branches of middle cerebral artery central branches of anterior cerebral artery
Thalamus	Branches of posterior cerebral, posterior communicating and basilar arteries
Hypothalamus striate	Anteromedial and posteromedial branches from the circle of Willis
Midbrain posterior	Basilar, superior cerebellar and cerebral arteries
Pons	Basilar, anterior inferior, and superior cerebellar arteries
Medulla	Vertebral, basilar, anterior and posterior spinal and posterior inferior cerebellar arteries
Cerebellum	Posterior inferior, anterior inferior, and superior cerebellar arteries

SPINAL CORD

The spinal cord extends from the foramen magnum to the interspace between the first and second lumbar vertebrae in adults and still lower down in infants and children. Though the cord stops at this level the arachnoid mater extends down to the second sacral vertebra and the dura mater extends a bit further down.

31 pairs of spinal nerve roots emerge from the cord. The segments in the cord are:

- Cervical 8
- Thoracic 12
- Lumbar 5
- Sacral 5
- Coccygeal 1

From each segment the anterior nerve root emerges and carries motor fibers to the periphery (Fig. 31.3). Posterior sensory root joins at each segment, and this carries sensory information to the cord from the peripheral receptors, through the peripheral nerves. The anterior and posterior nerve roots join to form a spinal nerve. The roots emerge through the intervertebral foramina. At the cervical and thoracolumbar regions the cord is wider since the roots for the brachial and lumbosacral plexus arise at these levels. Since the spinal cord is shorter than the spinal canal, the spinal segments and the vertebrae do not correspond numerically.

The spinal segment corresponding to each vertebra is given in Table 31.2.

The lower end of the spinal cord tapers to form the conus medullaris. The spinal roots below L1 pass down for varying distances in spinal canal to emerge at their respective intervertebral foramina these constitute the cauda equina.

Blood Supply to Spinal Cord

The upper part of the spinal cord is supplied by branches of the vertebral arteries through the posterior and anterior spinal arteries. These arteries course down along the dorsal and ventral surfaces of the medulla oblongata. The right and left anterior spinal arteries unite to form a single midline arterial channel, which descends down in the median fissure of the spinal cord. Each posterior spinal artery divides into two branches which descend on the lateral surfaces of the spinal cord, ventral and dorsal to the dorsal nerve roots, forming two posterior longitudinal arterial plexuses on either side. The anterior midline arterial channel and the two posterior arterial plexuses are reinforced by anterior and posterior radicular arteries. These radicular arteries, which arise at irregular intervals from the ascending cervical, deep cervical, intercostal, lumbar and sacral arteries, pass along with the spinal roots to enter the spinal canal.

Table 31.2: Spinal segment corresponding respective vertebra

Vertebral body level	*Spinal segment*
Cervical vertebrae	add 1
Dorsal vertebrae 1–6	add 2
Dorsal vertebrae 7–9	add 3
10th dorsal vertebra	L_1 and L_2
11th dorsal vertebra	L_3 and L_4
12th dorsal vertebra	L_5
Ist lumbar vertebra	Sacral and coccygeal segments

One such artery (artery of Adamkeiwicz) which arises from the left side of the descending aorta in the lumbar region is particularly large. It is clinically more important because it forms a major source of blood supply to the lower two-thirds of the spinal cord. The upper thoracic (T_1 to T_4) and the upper lumbar (L_1 and L_2) segments of the spinal cord are more vulnerable to ischemia being in the border zones of the vascular territories. The anterior two thirds of the spinal cord receives blood supply from the branches of the anterior spinal arterial blood supply from the branches of the anterior spinal arterial channel, while the posterior one-third is supplied by branches from the posterior arterial plexuses. Often there is overlap. The outer most portions of the spinal cord are supplied by small arteries arising from the arterial plexus running on the pia mater.

The venous drainage of the spinal cord is by the spinal veins which usually course along with the spinal arteries and form the epidural venous plexus. At each intervertebral space, the epidural venous plexus communicates with the external vertebral venous plexus. Venous blood from the spinal cord flows upwards and drains directly into the systemic venous system through the vertebral veins. Due to absence of valves in the venous system, blood can flow in either direction across the communicating veins.

Knowledge of the vascular anatomy is essential to understand the vascular lesions that may affect the spinal cord. Occlusion of the anterior or posterior spinal arteries produce characteristic neurological deficits. Embolism arising from infective endocarditis, or air embolism occurring in deep sea divers may affect the spinal cord. Ischemia of the lower part of the spinal cord secondary to atherothrombotic disease of the aorta produces features of intermittent claudication of the lower limits.

MENINGES

Dura mater covers the brain and spinal cord and it is attached to the bony structures at the entry and exit of blood vessels and nerves. The arachnoid mater lines its inner surface. Subarachnoid space contains cerebrospinal fluid. The pia mater invests the brain and spinal cord closely. Blood vessels run on the pia mater and penetrate the surface, pass deep and supply deeper structures. A sheath of pia is carried down alongwith these vessels. This constitutes the Virchow-Robin space. Since the arteries are closely related to the meninges, lesions such as meningitis may lead to thrombotic occlusion of blood vessels supplying the neural structures.

CEREBROSPINAL FLUID

Normal amount of cerebrospinal fluid (CSF) in an adult is 130 to 150 mL. It is secreted by the choroid plexuses in the lateral, third and fourth ventricles. It passes into the subarachnoid space through the foramina on the roof of the fourth ventricle—foramina of Magendie and Luschka. It circulates around the brain and spinal cord and is reabsorbed into the dural venous sinuses through the arachnoid villi. Normal pressure of CSF when measured with a manometer connected to a lumbar puncture needle, which the subject lying on his side, fully relaxed, varies from 50 to 150 mm of water. Rise in intrathoracic and intra-abdominal pressures occurring during coughing, sneezing and straining at stools is promptly reflected as rise in CSF pressure. In severe dehydration, CSF pressure may fall. The brain is suspended in CSF and in this situation the brain weighs only 50 g.

The term blood-brain barrier is used to denote the phenomenon by which several substances present in blood (including drugs) fail to reach the neurons and cerebrospinal fluid. This has implications in the pathogenesis of diseases and in therapy.

SYMPTOMATOLOGY IN NEUROLOGICAL DISORDERS

A precise clinical diagnosis in neurology essentially depends on proper elicitation and interpretation of the symptoms and the physical signs The diagnosis should include the identification of the diseased structures, their functional impairment and possible pathology. Assignment of the site of the disease is called neurological localization. The nature of the lesion can be inferred from the order in which symptoms appear and progress.

Localization of the lesion is relatively easy and accurate at the peripheral levels in the nervous system because here the structural and functional organization is sharply defined and less modifiable by compensatory factors. Localization is less precise when the symptoms and signs are due to damage to the conducting pathways, subcortical masses of gray matter or cerebral cortex, because here compensatory mechanisms from other unaffected nervous structures may alter the clinical picture.

Neurological disorders may give rise to negative symptoms, i.e. loss or impairment of function, e.g. paralysis or anesthesia, or positive symptoms, e.g. convulsion or pain. Positive symptoms are generally due to irritative lesions whereas negative symptoms arise from destructive lesions. At times positive symptoms may occur in destructive lesions as well due either to release of some structures from inhibition, e.g. spasticity in UMN lesion and dyskinesia in Parkinson's disease.

The nature of the symptoms depends on several factors. These include:

1. The disease process, whether it is localized or diffuse
2. Whether it is a systemic disease affecting the nervous system secondarily
3. Its mode of onset
4. Rate of development or progression
5. The vulnerability of different elements of the nervous tissue to the pathological process.

Acute lesions like infection, hemorrhage, infarction or trauma affect all neural structures regardless of their structure and function, leading to complete or partial loss of function of the injured parts. These are most severe immediately after the onset, but partial or full recovery may take place as time passes. Slowly progressive localized lesions like tumors or other space occupying lesions, on the other hand, usually cause less severe symptoms which evolve gradually over a period of time.

Diffuse diseases like vascular lesions or demyelination cause incomplete damage to wide-spread areas and produce symptoms similar to acute localized lesions or more diffuse symptoms. Many others cause extensive damage, but predominant

or selective involvement occurs in certain functionally related systems, e.g. the affection of pyramidal tracts and anterior horn cells in motor neuron disease, lenticular nucleus and cerebellum in Wilson's disease, and posterior columns and pyramidal tracts in pernicious anemia.

Different tissues of the CNS vary in their susceptibility to disease processes. Ischemia affects the gray matter more than the white matter of the brain. In diffuse diseases of the brain, the highly evolved and differentiated functions are the ones to be affected first and more severely. Motor fibers in the white matter of the spinal cord or in mixed peripheral nerves are more vulnerable to compression than the sensory fibers. In nutritional and toxic diseases of the peripheral nerves, longer nerve fibers to the lower limbs are the earliest to be affected. All these factors play their role to affect the resultant damage to the nervous structures in various disease entities.

MOTOR FUNCTIONS (FIG. 31.1)

Motor activity may be divided into voluntary, reflex and automatic. Voluntary action is the one initiated, modulated and terminated at will by the individual. Reflex activity is brought on by appropriate sensory stimuli which activate reflex pathways which consist of the central neurons in the brainstem or spinal cord segments, an afferent pathway and an efferent pathway which innervate the corresponding muscle, e.g. light reflex, accommodation reflex, cough reflex, knee reflex, plantar response, micturition reflex and others. These reflexes may be mediated by the somatosensory system, e.g. spinal and brainstem reflexes or the autonomic nervous system, e.g. visceral reflexes.

Voluntary activity is controlled by the upper motor neuron which consists of cortical motor neurons and their axons which pass down to arborise with the nuclei situated in the brainstem or spinal cord. The corticospinal fibers arise from the cells of the cerebral cortex, pass down in the corona radiata, occupy a small area in the posterior one-third of the posterior limb of the internal capsule, form the crus cerebri in the midbrain and pass down the brainstem to reach the various levels of the spinal cord. In the pons these fibers are dispersed and are criss-crossed by transverse fibers. Within this meshwork lie the neurons of the reticular activating system. The motor nuclei of all the cranial nerves situated in the brainstem are supplied by corticobulbar fibers crossing over from the opposite side at different levels. In the medulla the fibers are again grouped together as the pyramids. More than 80% of these fibers cross to the opposite side at the lower border of the

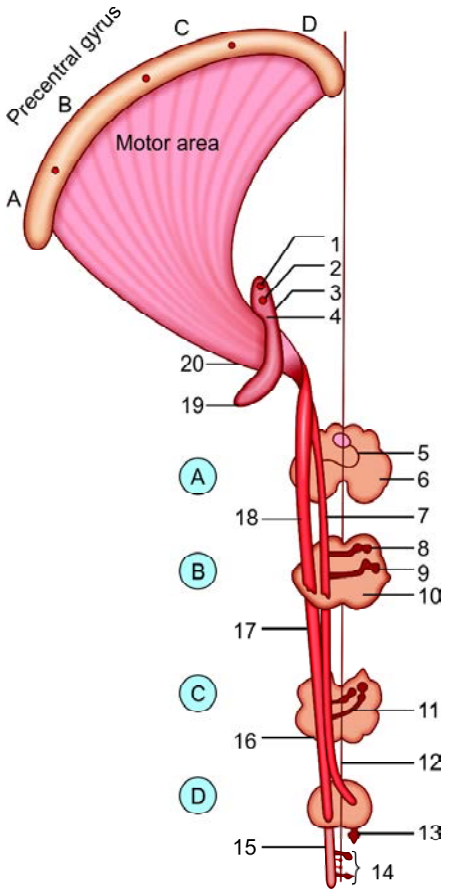


Fig. 31.1: Motor pathways: A-Cortical area representing head. B-Cortical area representing upper limb. C-Cortical area representing lower trunk, D-Cortical area representing lower limb

A. Midbrain, B. Pons, C. Medulla, D. Spinal cord

1. Visual fibers
2. Sensory fibers
3. Posterior limb of internal capsule
4. Fibers for lower limb in internal capsule
5. Fibers to opposite midbrain nuclei
6. Cerebral peduncle (crus cerebri)
7. Fibers for head in pons
8. 6th nerve nucleus
9. 7th nerve nucleus
10. Ventral aspect of pons
11. Fibers to opposite medullary tract
12. Oecussion of pyramidal nuclei
13. Lateral (crossed, indirect) corticospinal tract
14. Pyramidal fibers of direct tract crossing to supply opposite spinal nuclei
15. Anterior (direct corticospinal tract)
16. Medullary pyramid
17. Corticospinal (pyramidal) tract
18. Fibers for lower limb in pons
19. Anterior limb of internal capsule
20. Fibers for head in internal capsule

medulla to pass down as the crossed pyramidal tract and arborise at the anterior horn cells of the same side. The rest of the fibers descend on the same side (uncrossed pyramidal tract) and at different levels cross over to the opposite side to arborise at the spinal anterior horn cells (lower motor neuron-LMN). Thus the upper motor neuron exerts influence on the opposite side of the body at all levels.

Paralysis

The term "paralysis" denotes abolition of function either motor or sensory, but in common clinical parlance, this term is used to denote loss of motor function. The terms "paralysis" "plegia" and "palsy" are used to denote total or severe loss of motor function. "Paresis" denotes slight or partial loss of motor function.

Paralysis of voluntary muscles can occur either due to a lesion in the upper motor neuron (UMN) pathways or due to a lesion in the lower motor neuron (LMN) pathways. Tables 31.3 and 31.4.

In lesions of the UMN, only voluntary movements are abolished whereas reflex activity is preserved, or (even exaggerated). Lesion in the UMN may affect any part from the cerebral cortex to the terminal ramifications of the pyramidal fibers.

In lesions of the LMN, both voluntary and reflex activities are abolished. LMN paralysis may result from lesions occurring anywhere in the lower motor unit, i.e. anterior horn cell, efferent axon, its neuromuscular junction and the muscle. Antomically the site of lesion may be:

a. Anterior horn cells
b. Anterior spinal roots
c. Nerve trunks and plexuses
d. Peripheral nerves
e. Neuromuscular junction, or
f. Muscles (Table 31.5).

SENSORY FUNCTION

All sensations depend on impulses elicited by adequate stimulation of the sensory receptors. These impulses are transmitted to the brain by afferent sensory nerve fibers. All receptors which respond to external stimuli are called exteroreceptors. These are present in the skin, mucous membranes and the organs of special senses. The receptors that respond to stimuli from within the body are called inter oreceptors. These include proprioceptors in the muscles, ligaments and joints that respond to movements and changes in the position of the body and visceral receptors. Appreciation of particular sensations does not depend entirely on the stimulation of specific sensory nerves, but it is determined by the particular pattern of impulses that are received by the brain. For practical purposes the following types of receptors and their functions are given below:

- Touch — Free nerve endings, nerve endings in the hair follicles, Meissner's corpuscles, Merkel's disks
- Pain — Free nerve endings

Table 31.3: Clinical features of UMN and LMN types of paralysis

	UMN type	*LMN type*
Paralysis	Partial or total	Partial or total
Pattern of paralysis	Composite movements, especially fine, skilled voluntary movements in the distal parts of the limbs are affected rather than individual muscles	Individual muscle or muscle groups are affected
Muscle bulk	Unchanged, except due to disuse atrophy	Decreased (atrophy)
Fasciculations	Absent	May be present
Muscle tone	Increased (spasticity)	Decreased (flaccidity)
Deep tendon reflexes	Exaggerated, except in the acute stage of paralysis (neural shock)	Diminished or lost
Superficial reflexes		
a. Babinski sign	Present	Absent
b. Abdominal reflexes	Lost, if the UMN lesion is above 6 level	Preserved, unless the LMN lesion interrupts the corresponding reflex arc
c. Cremasteric reflexes	Absent, if the UMN lesion is above L_1 level	Preserved, unless the LMN lesion involves the reflex arc

Table 31.4: Guidelines to localize the site of lesion in UMN pathways

Cerebral cortex	Restricted contralateral paralysis, e.g. face, upper limb or lower limb. Focal seizures and cortical type of sensory loss, i.e. loss of tactile localization, tactile discrimination and steriognosis on the opposite side. Aphasia, apraxia, agnosia, if dominant hemisphere is affected
Internal capsule	Dense contralateral paralysis, e.g. hemiplegia hemianesthesia, contralateral, homonymous hemianopia
Thalamus	Impairment of all modalities of sensation, spontaneous pains and choreoathetosis on the opposite side.
	Note: These features constitute thalamic syndrome.Thalamic lesion in not associated with motor weakness, unless the lesion extends to the adjacent internal capsule
Midbrain	Paralysis of ipsilateral III and IV cranial nerves and contralateral hemiplegia
Pons	Paralysis of ipsilateral V, VI and VII cranial nerves and contralateral hemiplegia
Hemisection of spinal cord (Brown-Sequard syndrome)	Ipsilateral LMN paralysis involving the damaged segment UMN paralysis below this level. Band of hypoesthesia at the level of lesion. Loss of tactile discrimination, vibration and proprioception below the level of lesion. Contralateral loss of touch, pain and temperature below the level of lesion.
Complete transection of spinal cord	Bilateral LMN type paralysis at the affected segments, if the lesion affects the cord at a distinct level. Bilateral UMN type paralysis below the level of the lesion. Loss of all modalities of sensations below the level of the lesion. Bladder and bowel dysfunction

- Temperature — Free nerve endings, Krause's corpuscles, Ruffini's corpuscles
- Pressure — Pacinian corpuscles
- Proprioception — Neuromuscular spindles, neurotendinous spindles

Information from the peripheral sensory receptors is transmitted to the brain by a series of neurons, and it is of two types. These include conscious sensory information transmitted to the cortex via the thalamus, and which is appreciated as sensations, and sensory information which is transmitted to the cerebellum to coordinate muscle activity without reaching consciousness. Some of this unconscious sensory information is received by the spinal cord to mediate local reflex activity, midbrain for visual reflexes and to the other parts of the brainstem to activate the reticular activating system.

The conscious sensory information reaches the cerebral cortex through a series of three neurons, the first, second and third order neurons, while the unconscious sensory information is carried through only two neurons of first and second order. The first order neurons have their cell bodies in the posterior root ganglia. The second order neurons have their cell bodies either in the posterior horns of the spinal cord or in nucleus gracilis and cuneatus in the medulla oblongata. The third order neurons lie in the ventral posterolateral nucleus (VPL nucleus) of the thalamus. Ascending sensory pathways in the spinal cord carry different sensation for appreciation either in the thalamus or the cerebral cortex. Fig. 31.2 shows the position of various tracts (both motor and sensory) in the spinal cord.

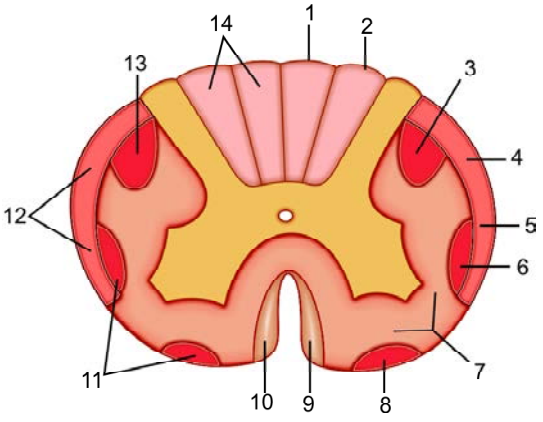


Fig. 31.2: Cross-section of spinal cord are:

1. Fasciculus gracilis
2. Fasciculus cuneatus
3. Lateral (crossed) pyramidal tract
4. Posterior spinocerebellar tract
5. Anterior spinocerebellar tract
6. Lateral spinothalamic tract
7. Extrapyramidal tracts
8. Anterior spinothalamic tract
9. Anterior (uncrossed) pyramidal tract, Functional representation
10. Voluntary movement
11. Pain, temperature and half touch
12. Equilibration
13. Voluntary movement
14. Position sense, vibration sense, half touch

Central Pathways for Different Sensations (Figs 31.3 and 31.4)

Light Touch

This is carried by the posterior column. First order neurons are in the posterior root ganglia. Their central axons in the posterior root enter the posterior white column in the same side and divide into long ascending and short descending branches. The long ascending fibers pass upward ipsilaterally

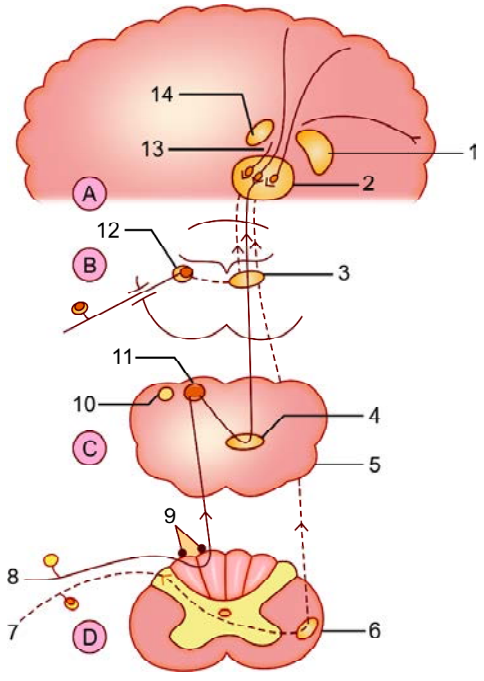


Fig. 31.3: Sensory pathways:
A. Cerebral cortex B. Pons C. Medulla D. Spinal cord
1. Lentiform nucleus,
2. Thalamus
3. Medial lemniscus and spinothalamic tract
4. Medial lemniscus
5. Spinothalamic tract
6. Spinothalamic tract
7. Posterior nerve roots forming the spinothalamic tract
8. Posterior nerve roots forming the posterior columns
9. Posterior columns
10. Nucleus cuneatus
11. Nucleus gracilis
12. Fifth nerve nucleus
13. Internal capsule
14. Caudate nucleus

in the dorsal white column as fasciculus gracilis medially, and fasciculus cuneatus laterally. They carry sensations from the lower and upper parts of the body respectively. Axons of the second order neurons cross the midline after relay in the nucleus of fasciculus gracils and cuneatus and ascend up in the medulla, pons and the midbrain as the medial lemniscus and terminate in the third order neurons situated in the VPL nucleus of the thalamus. Axons of the third order neurons ascend up in the posterior limb of the internal capsule and the corona radiata to terminate in the sensory cortex.

Touch

This is carried by the anterior spinothalamic tract. First order neurons lie in the posterior root ganglia. Their central axons in the posterior roots enter the posterior hom and ascend up one or two segments before terminating on the second order neurons in

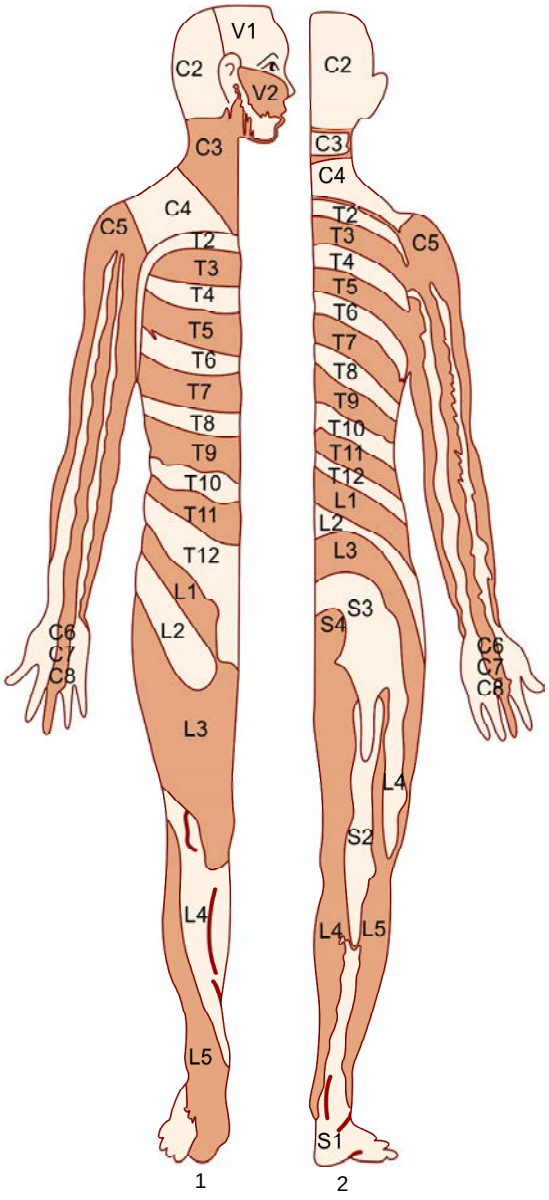


Fig. 31.4: Dermatomes. Segmental innervation: (1) Front, (2) Back

the substantia gelatinosa. The axons of the second order neurons cross the midline to the opposite side and ascend up as anterior spinothalamic tract in the anterolateral column of white matter. In the medulla, pons and midbrain it ascends up together with the lateral spinothalamic tract, and terminates in the third order neurons situated in the VPL nucleus of the thalamus. The axons of most of the third order neurons pass up through the posterior limb of the internal capsule and the corona radiata to reach the sensory cortex. In the anterior spino-

Table 31.5: Guidelines to localize the site of LMN lesion

Clinical feature	*Anterior liotin cells in spinal cord*	*Anterior nerve roots*	*Nerve trunks and plexuses*	*Peripheral nerves*	*Neuromuscular Muscle junction*		*Comments*
Pattern of weakness	Patchy or asymmetrical	Muscles Supplied by roots	Muscles supplied by trunk or plexus asymmetrical	Distal and symmetrical asymmetrical in mononeuritis	Proximal and symmetrical	symmetrical	Relative symmetry in SMA
Atrophy of muscles	Early in acute Late in chronic	Early	Early	Early	Nil	Early or late	
Hypertrophy of muscle	Rare	Absent	Absent	Absent	Absent	May occur	
Fasciculations	Common	Less common	Rare	Rare	Absent	Absent	
Deep tendon reflexes	Absent or decreased	Absent	Absent	Absent	Absent	Decreased	Preserved in inflammatory disease of muscles
Power of muscle	Relatively good compared to atrophy	Weak	Weak	Weak	Weakness worsens with repeating motor action Fatigability	Weak	
Sensory deficit	Absent	Present in segmental distribution when posterior root is involved	Present in segmental distribution	Present	Absent	Absent	

thalamic tract, the fibers from the lower part of the body lie laterally and those from the upper part of the body, medially.

Pain and Temperature

These are carried up by the lateral spinothalamic tract. First order neurons are situated in the posterior root ganglia. Their central axons in the posterior roots enter the posterior horn and divide into ascending and descending branches. The ascending branches travel one or two segments up and arborise with the second order neurons in the substantia gelatinosa on the same side. The axons of these second order neurons cross to the opposite side and ascend up in the lateral white column as the lateral spinothalamic tract. The temperature fibers lie dorsally and medially whereas the pain fibers lie anteriorly. In the medulla, pons and midbrain it ascends up together with the anterior spinothalamic tract and terminates in the third order neurons present in the VPL nuclues of the thalamus. Axons of these third order neurons pass up through the posterior limb of the internal capsule and the corona radiata to reach the sensory cortex.

In the lateral spinothalamic tract, the fibers from the lower part of the body lie osterolaterally and those from the upper part of the body antero-medially.

Tactile Localization, Tactile Discrimination and Kinesthetic Sensations

Tactile localization, tactile discrimination and vibration sense, joint sense, position sense and sensation of passive movement are carried by the posterior column.

Pressure Sensation

This is carried by the anterior spinothalamic tract. Since different sensations are carried by different discrete tracts in the spinal cord some of which are crossed and others uncrossed, localized lesions of the spinal cord give rise to dissociated anesthesia, i.e. loss of one modality of sensation, while preserving another. For instance, in syringomyelia where the crossing pain and temperature sensory fibers are affected early and selectively, pain and temperature sensations are lost whereas touch and other posterior columns sensations are preserved.

The fibers carrying touch cross over to the opposite side more obliquely than those carrying pain and temperature. Due to this fact, in transection or hemisection of the spinal cord, the level of sensory loss may be different for touch, pain and temperature.

PROFILE OF NEUROLOGICAL DISORDERS IN INDIA

Clinical neurology is a chimera. It encompasses a great variety of neurological disorders, which may be congenital, hereditary, nutritional, vascular, inflammatory, infective, toxic metabolic, demyelinating, degenerative, traumatic or neoplastic. The central peripheral and autonomic components of the nervous system either selectively or in combination may be involved in various pathological processes. In addition, many primary systemic diseases also affect the nervous system secondarily during their course or as sequelae. The spectrum of neurological disorders in India is almost the same as in the West, though their incidence varies. Some of the common neurological problems encountered by the general physicians in India are briefly highlighted below.

Arbitrarily, these disorders can be broadly categorized into two groups:

i. Those with no or few neurological signs.
ii. Those with multiple neurological signs.

Those in the first group include headache, epilepsy, dizziness, pain in the neck, back and limbs and syncopal attacks which together, form the greater bulk of the patient material in general practice. An accurate diagnosis of the cause of these problems can be established only by a carefully elicited history, repeated physical examinations and appropriate investigations. Among all types of headaches, tension headache and migraine are the most frequent ones in all age groups. Though mild hypertension and diseases of eye, ear and paranasal air sinuses coexist in many patients with headache, they are seldom the primary cause for the symptom, though they certainly aggravate the distress. Among the various types of epilepsy, generalized tonic-clonic seizures is the most common type in children and adults. In neonates, hypoxicanoxic brain damage, intracranial hemorrhage and CNS infections are the major causes for convulsions, followed by hypoglycemia, hypocalcemia and inborn errors of metabolism. Brain tumors, tuberculomas, cysticercosis, cerebral infarcts and head trauma are the causes for symptomatic epilepsy. The common causes for dizziness or vertigo are diseases of the peripheral vestibular apparatus, postural hypotension or lesions of the cervical spine. Anemia and drug induced giddiness should be kept in mind while analyzing the problem of giddiness. Of all the pains that affect either the neck, low back or limbs, those due to musculoskeletal disorders top the list. Spondylosis and prolapsed intervertebral disc in the cervical or lumbar region are common among the demonstrable causes.

The second group of neurological disorders which are accompanied by demonstrable neurological deficits can be classified as follows:

Developmental defects: Serious developmental defects of the nervous system invariably result in death of the fetus in utero or shortly after birth. Minor defects may not be clinically evident. Moderately severe defects lead to neurological disabilities in later life. These include neural tube defects evident at birth or soon afterwards, congenital hydrocephalus in children and a variety of craniovertebral anomalies such as basilar invagination, Arnold-Chiari malformation, congenital atlantoaxial dislocation, other abnormalities of cervical spine and syringomyelia.

Infections: Meningitis, encephalitis, poliomyelitis, herpes zoster, cerebral malaria and suppurative infections form the main bulk of neuro infections. Bacterial meningitis due to *pneumococcus*, *Meningococcus*, and *H. influenzae* is still common in all age groups. Gram-negative meningitis due to *E. coli* and others occur in neonates. Tuberculous meningitis has to be considered in every case of subacute or chronic meningitis. Syphilitic meningitis may be seen at times. Fungal meningitis due to *Cryptococcus neoformans*, *Aspergillus* and *Mucor* should be considered in immunocompromised individuals. Encephalitis and meningoencephalitis, caused mainly by viruses are also common. In many cases the nature of these viruses is not known. Japanese B encephalitis, herpes simplex encephalitis, encephalitis due to rabies and measles are identifiable viral infections. Encephalitis may also occur as a complication during systemic viral infections. Poliomyelitis incidence has come down remarkably in several communities as a result of

vaccination. AIDS related neurological problems, should always be kept in mind. Cerebral malaria and neurocysticercosis are frequently seen in many parts of the country.

Vascular lesions: Stroke or cerebrovascular accident is the most common cause for any sudden focal neurological deficit. Among the two common types of stroke, occlusive vascular disease leading to cerebral infarction is more common than hemorrhagic strokes.

Age above 60 years, diabetes, hypertension and atheroscleros are the predisposing factors for occlusive cerebrovascular disease. Cerebral embolism and primary subarachnoid hemorrhage are seen mainly in younger individuals. Cerebral embolism in the young is most commonly associated with rheumatic or congenital heart disease and infective endocarditis. Atrial fibrillation due to mitral stenosis and mural thrombosis after myocardial infarction are the other common causes of cerebral embolism. Atheromatous lesions of the carotid arteries in the neck leading to cerebral embolism are seen in the middle aged and elderly individuals. Hypertension is the most common cause of intracerebral hemorrhage in all age groups. Berry aneurysms in the circle of Willis and cerebral arteriovenous malformations are the most common causes of primary subarachnoid hemorrhage in the young.

Nonspecific arteritis of carotid: Arteries and their intracranial branches, postpartum cortical venous thrombosis and chronic meningitis with arteritis are frequent causes of stroke in the young (below 40 years of age) in India. Hypertensive encephalopathy and vascular dementia are also common. Comparatively, vascular diseases of the spinal cord are less common.

Demyelinating disorders of the two forms, namely primary form, e.g. multiple sclerosis and Guillain-Barre syndrome and secondary form seen in association with viral infections, vaccinations and exanthematous fevers and others, primary forms are less common compared to secondary forms. They present as optic neuritis, acute encephalomyelitis, transverse myelitis and acute polyradiculoneuritis.

Degenerative diseases: Parkinsonism, Alzheimer's type of dementia, motor neuron disease, spinal muscular atrophies and muscular dystrophies are the common degenerative diseases.

Miscellaneous disorders: Mental retardation due to birth injury and neonatal CNS infections, cerebral palsy, peripheral neuropathy due to diabetes, Hansen's disease and of undetermined etiology, coma due to metabolic and toxic causes are also commonly seen in general practice.

Neurological Disorders having Higher Incidence in India

Neurotuberculosis It is seen throughout the country. It is the greatest imitator of all diseases as it manifests in so many different ways.

i. Tuberculous meningitis, seen more commonly in children and younger age groups.
ii. *Intracranial tuberculoma,* which may be solitary or multiple, large ones, manifesting as intracranial space occupying lesions with progressive focal neurological deficits and raised intracranial pressure or small lesions frequently manifesting with focal convulsions.
iii. *Basal tuberculous meningitis,* manifesting as multiple lower cranial nerve palsies.
iv. *Optochiasmatic arachnoiditis* presenting as progressive bilateral visual failure.
v. *Chronic adhesive spinal arachnoiditis* manifesting as progressive myeloradiculopathy.
vi. *Tuberculosis of the spine,* presenting as Pott's paraplegia.

Neurocysticercosis

This is caused by invasion of the central nervous system by the larval form (cysticerci) of Taenia solium. Clinical manifestations include raised intracranial pressure, epilepsy and psychiatric symptoms. It occurs among vegetarians and nonvegetarians. It is more common in northern and central parts of India.

Neuroleprosy

This manifests either as mononeuritis, mononeuritis multiplex or polyneuropathy. The ulnar, median, radial, great auricular, common peroneal and sometimes facial nerves are affected. Cutaneous lesions of leprosy may not be prominent in some of these cases but they can be detected on scrutiny. It is seen in almost all parts of the country.

South Indian paraplegia (Syn tropical myelopathy): It is a condition of unknown etiology, affecting subacutely the spinal cord, with involvement of the pyramidal tracts and dorsal columns, peripheral sensory nerves and sphincters. Contrary to what the name suggests, it occurs all over the country.

Neurolathyrism

This is a condition seen in central and northern parts of the India in which there is subacute onset and slow progression of pure upper motor neuron type of paraplegia. It is caused by consumption of food grains contaminated with the seeds of Lathyrus sativus (Kesari dal) which is a drought resistant crop.

Fluorosis

This is widespread in many parts of India. Advanced disease presents with compressive myelopathy and radiculopathy.

Atypical forms of Motor Neuron Disease

i. Amyotrophic lateral sclerosis (ALS)-like condition in juvenile and young subjects.
ii. Pattern similar to ALS but with nerve deafness—Madras pattern of motor neuron disease.
iii. Purely LMN type of involvement of one extremity monomelic or segmental amyotrophy.

An epidemiological study in a rural district in West Bengal Saha SP et al (JIMA 2002.101, 299-304) reveal that in a population of 100,000 the frequency of neurological diseases were:

• Headache	870
• Vertebral diseases with neurological involvement	540
• Seizure disorders	360
• Vertigo	230
• Stroke	147
• Movement disorders	140
• Peripheral neuropathy	80

The general pattern of neurological diseases remain more or less the same even at present.

CHAPTER

32 Clinical Examination of the Nervous System

AS Girija, KV Krishna Das

Symptoms in neurology, General examination, Scheme of neurological examination, Higher functions, Level of consciousness, Glasgow coma scale, Assessment of higher functions, Speech and Language, *Cranial nerves:* Olfactory nerve, Optic nerve, Fundus examination, Oculomotor, Trochlear and abducent nerves, Test for ocular movements, Test of pupils, Test of squint, Tests for Diplopia, Nystagmus, Special types of Nystagmoid movements, Supranuclear mechanisms of eye movements, Trigeminal nerve Facial nerve, Vestibulocohlear nerve, Glossopharyngeal nerve, Vagus nerve, Accessory nerve, Hypoglossal nerve, Bulbar and pseudobulbar palsy, Stance and gait, Examination of motor system, Abnormal movements, Muscle power, Examination of reflexes, Muscle stretch reflexes, Superficial reflexes, Sensory system, Coordination, Physical signs of cerebellar dysfunction, Signs of meningeal irritation, Innervation of urinary bladder and disorders of micturition, Nervous control of rectum and defecation reflex, Neurological control of sexual function in male, Tests of autonomic function

INTRODUCTION

As in the case of all other systems, clinical examination starts with the history and proceeds on to general examination, systematic examination and investigations. Neurological disorders follow classic patterns of evolution, progress and resolution. Lesions at specific sites produce effects which are obvious at the periphery. Destructive lesions such as infection or inflammation lead to loss of function such as paralysis or anesthesia. Irritative lesions lead to convulsions, paresthesia or sensory equivalents of epilepsy.

History is most important to arrive at the etiological diagnosis and to suggest the possible pathological lesion. Great care should be taken in eliciting the history sequentially. The onset, evolution, recovery and residual disability should be enquired into. In most cases the history will take the physician to very near the diagnosis.

Three classical examples are given below:

1. An unvaccinated child developing fever with paralysis of one or more limbs on the second or third day of the illness is very suggestive of poliomyelitis.
2. A middle-aged diabetic going to bed as usual and found to be hemiplegic on waking-up in the morning, has probably developed cerebral thrombosis.
3. An adult developing retention of urine and weakness of the lower limbs, either during a course of antirabic vaccine treatment or within two to three weeks of its completion, is most probably developing post-vaccination myelitis.

Symptoms in Neurology

Neurological diseases may present with symptoms referable to lesions in the nervous tissue or symptoms referable to other organs, due to the intimate relationship between the nervous system and other systems. Most of such symptoms have been dealt with in the text in other sections. Common symptoms referable to nervous tissues are listed below (Table 32.1).

Headache, pain coma, epilepsy and vertigo-gidd iness complex are described in detail since these

Table 32.1: Common symptoms in neurological diseases

Site of lesion	*Symptoms*
Cerebral hemispheres	Impairment of mental function, alteration in consciousness, seizures, abnormalities of speech and language, hemiplegia, hemianesthesia, hemianopia, apraxia, agnosia
Frontal lobe	Apathy, lack of initiative, change in social behavior and personality, memory impairment, incontinence of urine and faces, anosmia
Parietal lobe	Dysphasia, dyscalculia
Dominant side	Dyslexia,
Nondominant side	Spatial disorientation, dressing difficulty
Temporal lobe dominant side	Dysphasia, dyslexia, impaired memory, hallucinations of smell, sound and vision
Nondominant side	Impaired memory, hallucinations
Occipital lobe	Visual impairment, visual hallucinations, inability to recongnize familiar faces
Basal ganglia	Abnormal movements of limb and jaw, bradykinesia, muscular rigidity
Cerebellum	Dysarthria, ataxia of limbs and staggering gait
Brainstem	Cranial nerve palsies, quadripiegia crossed hemiplegia with or without sensory deficit, bulbar or pseudobulbar palsy
Cranial nerves I	Loss of smell or perversion of smell
II	Abnormalities of vision
III, IV, VI	Diplopia, squint
V	Loss of sensation in the skin of the face and in the mucous membrane of nasopharynx, Difficulty in clenching the jaws and opening the mouth
VII	Facial paralysis, distortion of face, watering from eyes, inability to close the eye
VIII	Deafness, tinninuts, vertigo
IX to XI	Dysphagia, dysphonia, dysarthria, nasal regurgitation of fluids
XII	Weakness of tongue, wasting
Motor system	Weakness of limbs, wasting of muscles, fasciculations, spasticity
Sensory system	Pain, paresthesia, anesthesia, hyperesthesia, ataxia of gait
Sphincter disturbances	Urinary retention/incontinence, fecal retention/ incontinence, priapism, reflex ejaculation
Autonomic nervous system	Trophic changes, impotence, constipation diarrhea, urinary retention or incontinence, postural vertigo, syncopal attacks
Meninges	Headache, nuchal pain

are much more common to occur as the presenting symptoms in primary neurological diseases.

GENERAL EXAMINATION

Before proceeding to neurological examination specially look for:

State of consciousness and mental state: Metabolic disturbances such as diabetic ketoacidosis, hypoglycemia, uremia, hepatic failure and poisoning may give rise to abnormalities of consciousness and mental functions. These should be looked for.

Cardiovascular Findings

Examination of the pulse, blood pressure and the heart gives clues regarding the etiopathogenesis of several neurological disorders. Hypertension is associated with a high-risk of thrombotic and hemorrhagic strokes. Structural heart diseases such as valvular heart disease and congenital heart disease, arrhythmias such as atrial fibrillation, ischemic heart disease and infective endocarditis account for a high proportion of cerebrovascular complications.

Diabetes Mellitus

Several neurological complications can occur due to diabetes mellitus. These complications usually occur in patients known to have diabetes mellitus, but occasionally they may be the presenting manifestations. The neurological complications can be acute or chronic.

The acute complications are coma and convulsions due to severe hyperglycemia with or without ketoacidosis and hypoglycemia. The chronic complications are generally due to:

i. vascular or
ii. nonvascular causes.

Among the vascular complications are those caused by large artery disease (cerebrovascular disease). Microvascular complications are caused by small artery disease leading to mononeuropathies (cranial and peripheral nerves). Nonvascular complications are thought to be due to direct metabolic effect on the nerves. They include peripheral neuropathies and autonomic neuropathies.

Cyanosis

Cyanotic congenital heart disease may be complicated by brain abscess, paradoxical cerebral embolism, seizures and cerebral venous and arterial thrombosis. Cyanosis in respiratory failure may be associated with carbon dioxide narcosis.

Fever

Infective disorders of the central nervous system (CNS) such as meningitis, encephalitis and brain abscess are accompanied by fever. Even in the absence of direct involvement of the CNS, several systemic infections give rise to delirium which is a toxic confusional state, e.g. typhoid. Children and the aged are more prone to develop delirium. In children below the age of 5 years, febrile convulsions are common.

Nutrition

Several nutritional disorders affect the nervous system. Deficiency of thiamine leads to peripheral neuropathy, and Wernicke's encephalopathy. Deficiency of niacin and cyanocobalamin may give rise to disturbances of higher mental functions. In addition, vitamin B_{12} deficiency may be associated with subacute combined degeneration of the cord.

Lymph Nodes

Lymphomas, tuberculosis, leukemias, AIDS, syphilis and several other infections which present with generalized lymphadenopathy may affect the nervous system. Localized metastatic lymph nodes secondary to carcinoma lung may point to metastases in the brain or paraneoplastic neurological manifestations of malignancy.

Skin

Café-au-lait spots, naevi, neurofibromata and vascular malformation such as angiomatoses may all be associated with lesions in the brain, spinal cord, cranial nerves or spinal nerves. Sensory loss occurring in peripheral neuropathy, mononeuritis multiplex and syringomyelia may lead on to trophic ulcers and destructive lesions in the extremities.

Abnormalities of Skull

Microcephaly, hydrocephalus, asymmetry of the skull, metastatic deposits in the skull, areas of softening as is seen in myeloma and histiocytosis may all be associated with neurological lesions. In children with hydrocephalus with raised intracranial pressure, percussion over the skull may give rise to "cracked-pot-resonance".

Face

Several abnormalities point to neurological diseases. Facial asymmetry, hemiatrophy, pouting of lips and transverse smile in myopathies, mask-like facies of parkinsonism, acromegalic facies, vascular naevi in Sturge-Weber syndrome, and adenoma sebaceum in tuberous sclerosis are some of the many external markers of neurological disease. The facial abnormalities can be easily recognized by the physician at the first examination.

Eyes

Kayser-Fleisher rings which suggest Wilson's disease, proptosis, pulsatile exophthalmos and specific neurological abnormalities such as paralysis, strabismus and nystagmus should be looked for.

Substance abuse

Several substances which cause addiction lead to acute and chronic damage to the nervous system. Prominent among them are:

Alcohol	Tremors, varying grades of altered consciousness, peripheral neuropathy, cerebellar dysfunction, delirium tremens on alcohol withdrawal.
Phenothiazines	Akathisia, i.e. inability to sit quiet, associated with a feeling of restlessness and anxiety, dystonias, secondary parkinsonism, seizures and others.
Excessive smoking of tobacco	Tremors, restlessness, insomnia

Scheme of Neurological Examination

After performing the general examination, proceed to examine the nervous system in the following order so that physical signs are not missed and the whole process is completed within the minimum time without tiring the patient unduly.

1. Higher mental functions: Consciousness, orientation, memory, intelligence, speech, sleep.
2. Cranial nerves including funduscopy.
3. Motor system
4. Sensory system
5. Reflexes
6. Cerebellar functions
7. Stance and gait
8. Head and spine
9. Signs of meningeal irritation
10. Autonomic functions

Absence of certain physical signs may be as important as the presence of others for diagnosis and therefore these should also be recorded. For example, when confronted with a patient presenting with wasting of the hand muscles, absence of any sensory abnormality suggests the possibility of motor neuron disease or primary myopathy in contrast to peripheral neuropathy.

While eliciting physical signs even slight deviation from normal should be noted and recorded because this may be the early indication of progressive neurological disease. For example, even a minor abnormality of the plantar response on one side with normal flexor plantar response on the opposite side may be the only early evidence of dysfunction of the corticospinal pathways even when the muscle power, tone and muscle stretch reflexes are unaffected.

The manner in which a motor action is performed by the patient should be noted and recorded even when he is able to achieve the intended goal. For instance, in paralysis of proximal muscles of a limb the patient may still be able to move the paralyzed limb by employing trick movements, but not in the normal way.

HIGHER FUNCTIONS

Syn: Mental or Intellectual Functions

After general examination the student should start with the examination of higher functions. Disturbances of higher functions may occur directly from a focal or diffuse organic brain disease or indirectly from the emotional reactions to the illness or from a combination of the two. Psychiatric disorders also affect the higher functions considerably. Higher functions include level of consciousness, intellectual performances, emotional state, thought processes, complex sensory perceptions, complex motor acts, speech and language.

Proper evaluation of higher functions is possible only when the person is alert and attentive with normal comprehension. Several elaborate tests have been described for evaluating higher functions under particular circumstances. For initial screening a short, quick and concise "minimental state examination" may be done in all cases. If the screening test is normal, further detailed testing is not usually necessary and the student can proceed with the rest of the neurological examination. But if the screening test is abnormal, detailed mental status examination has to be done. Assess the level of consciousness before proceeding with further examination.

LEVEL OF CONSCIOUSNESS

Fully Conscious State

An individual is termed as "conscious" in the narrow limits of clinical terminology when he is aware of himself and his surroundings during wakefulness. In this state, a normal person is fully alert, oriented to his surroundings and responds appropriately to external stimuli which may be auditory, verbal, visual, tactile or painful. His speech is normal and he has normal voluntary motor activity. His eyes are open with intermittent blinking and his eye movements are normal. Consciousness is maintained by the reticular activating system in the brainstem, through its thalamocortical projections as a result of constant flow of sensory inputs from the sense organs.

Confusional State

i. Inability to think with customary speed and clarity, leading to impairment of problem—solving ability and coherence of ideas about a subject.
ii. Inability to carry out more than simple commands.
iii. Loss of awareness of the surrounding environment.

iv. Inability to sustain long conversation, with frequent drifting from one topic to another.
v. Disorientation in time and place.

Note: At times a patient with Wernicke's dysphasia may mimic confusion state. This has to be borne in mind.

Somnolence

A somnolent person appears to be asleep, but he can be aroused transiently by verbal or painful stimuli and made to perform simple motor tasks and appropriate verbal responses, but immediately he drifts back into a sleeplike state when the stimulus is stopped.

Stupor

The patient who appears to be asleep can be aroused transiently only by vigorous and repeated painful stimuli. When aroused, the eyes are opened but spontaneous eye movements will not be present. Response to simple verbal commands is either slow and inadequate, or absent. Restlessness and spontaneous stereotyped movements are common. He immediately drifts back into sleep-like state when the stimulus ceases.

Semi-coma

It is the lighter stage of coma in which painful stimuli, shaking, or shouting will cause transient stirring movements, moaning or muttering, and quickening of respiration. As soon as the stimulation ceases the patient drifts to his original state. Most of the superficial and muscle stretch reflexes may be elicitable and plantar responses may be either flexor or extensor.

Sleep

Sleep is a physiological state of unconsciousness in which the pulse and the respiratory rate fall, the eyes deviate upwards, the pupils are constricted but reactive to light, the muscle-stretch reflexes are absent and the plantar responses become extensor. Sleep differs from abnormal alterations of consciousness in that the subject can be easily woken up with verbal or tactile stimuli and he resumes normal mental function promptly.

Normal sleep occurs in 5 stages. The first 4 stages (I to IV) are called nonrapid eye movement (NREM) sleep and the fifth-one, rapid eye movement sleep (REM). These stages are identified by simultaneous recording of EEG, EMG and electro-oculogram; this combination is called polysomnogram. When a person falls asleep he passes through stages I to IV of NREM sleep which takes about 70 to 100 minutes, followed by REM sleep for the next 25 to 30 minutes. After this again stage I of NREM begins. This cycle of NREM-REM sleep is called a sleep cycle and usually 4 to 6 such sleep cycles are repeated in a night's sleep in a healthy adult. However, the duration and the number of sleep cycles vary with age and sex. Stage I of NREM is called drowsiness and stage II, light sleep. Stages III and IV of NREM sleep and REM sleep are called deep sleep. During drowsiness and light sleep, the muscle tone in the limbs is maintained, there may be gross body movements but no eye movements. In the deep sleep stage of NREM also, there will not be any eye movements, the limb tone is maintained, and there may be gross limb movements. In the REM sleep, there will be conjugate eye movements, but the limbs are hypotonic, the person will be still, with small twitching and tremulous movements in the face, hands and feet. Normal sleep is essential to maintain functional normalcy and normal neurological reactions. Prolonged insomnia leads to abnormality of higher functions and psychological behavior. Adequacy of sleep for each individual depends on the duration and depth of sleep.

Coma

It is a state of deep unconsciouness from which he cannot be aroused even by painful stimuli. Sometimes, these painful stimuli may result in reflex decorticate or decerebrate postures. The superficial and muscle stretch reflexes are usually absent. Plantar response is extensor.

Note: Painful stimulus is usually applied in one of the following ways:
1. Pressure behind mastoid process, and
2. Rubbing firmly over the sternum or pressure over any bony point.

Decerebrate Posture Rigidity

A patient usually in coma caused by structural lesions in the brain such as tumor, hemorrhage, infarct and others may assume this posture unilaterally or bilaterally either spontaneously or in response to painful stimuli. This is characterized by tonic

extension and internal rotation of the upper extremity and tonic extension and plantar flexion of the lower extremity associated with jaw clenching and head retraction. It is important to recognize this grave sign because it indicates dysfunction of upper brainstem between the superior colliculus of the midbrain and vestibular nuclei in the pons. In metabolic and drug induced coma, this posture does not develop.

Decorticate Posture Rigidity

This posture is characterized by tonic flexion of the forearms at the elbow, adduction and flexion of the arm at the shoulder and flexion of the fingers, with tonic extension of the lower extremity, either on one or both sides. This is seen in lesions above the brainstem, affecting the cortex or the corticospinal tracts. Like decerebrate posture, this also occurs in coma and in chronic stages of hemiplegia.

Delirium

It is a state of confusion with excitement, agitation, vivid hallucinations and tremulousness. It is caused by cerebral dysfunction, but it is different from confusion, stupor, semicoma and coma. When a patient slowly lapses into coma he passes through the stages of confusion, stupor and semicoma. During recovery from coma this sequence is reversed. A delirious patient usually does not pass into coma, but hepatic coma is an exception.

GLASGOW COMA SCALE

This scale is commonly employed to evaluate the degree of coma resulting from head trauma or cardiorespiratory arrest. It correlates well with prognosis for recovery and also helps to plan emergency management. In coma due to many medical conditions, its application and correlation with prognosis is less clear.

To arrive at the coma "score", three parameters are tested and scored as given below. The total score may range from 13 to 15. The best score is 15 indicating normalcy. The worst is 3 indicating very poor prognosis for life and recovery. The higher the score, better is the prognosis for recovery and favorable response to treatment.

Opening the eyes
- Never 1
- To painful stimuli 2
- To verbal stimuli 3
- Spontaneously 4

Best verbal response
- No response 1
- Incomprehensible sounds 2
- Inappropriate words 3
- Disoriented and converses confusedly 4
- Oriented and clear converzation 5

Best motor response
- No response 1
- Extension (decerebrate rigidity) 2
- Flexion abnormal (decorticate rigidity) 3
- Flexion withdrawal 4
- Localizes pain 5
- Obeys to verbal commands 6

ASSESSMENT OF HIGHER FUNCTIONS (COGNITIVE STATE)

Two standardized questionnaires, help to assess the mental state rapidly. These include mental status questionnaire (MSQ) and minimental state examination (MMSE).

Mental Status Questionnaire (MSQ)

For each of the following question 1 point is given:

1. What is the name of this place (where are we now)?
2. What is the address of this place?
3. What is the date?
4. What month is it?
5. What year is it?
6. How old are you ?
7. When is your birthday?
8. What year were you born?
9. Who is the Prime Minister?
10. Who was the previous Prime Minister?

Interpretation

Normal subjects should be able to answer 9 questions correctly. Less than 8 suggests cognitive impairment.

Minimental State Examination (MMSE)

This is a simple test that can be administered easily and quantified. Minimental state examination (MMSE) discriminates between mild, moderate and severe derangements in higher functions. Major aspects of higher functions are assessed by asking questions

Table 32.2: Minimental state examination

Function tested and how to test	Score
1. Orientation (Score 1 for each correct answer) Ask the following 10 questions • What is the current year? • What month is it? • What is the date today? • What day of the week is today? • What season of the year is it now? • What is the name of this hospital? • What floor of the hospital you are in now? • What is the name of this city? • What is the name of this state? • What is the name of this country?	0-10
2. Registration (Score 1 for each correct answer) • Tell him the names of 3 unrelated objects clearly, loudly, and taking one second to say each word, and then ask him to repeat all 3 in the first trial itself. (e.g. (1) Temple, (2) Book, and (3) Orange) *Note:* Patient will be required to recall the names of these 3 objects at a later stage, when the ability to recall is tested. So, ask him to remember the three names. If necessary, repeat the names up to 6 times and ask him also to repeat. If he cannot repeat at the end of 6 trials, recall cannot be tested meaningfully at a later stage.	0-3
3. Attention and calculation (Score 1 for each correct serial response) • In a patient who knows calculations ask him to subtract 7 serially from 100 up to 65 (5 subtractions–1 score for each). • In a patient who has not learned calculations tell him a five lettered word in his native language (e.g. India) and ask him to spell the word backwards (e.g. India).	0-5
4. Recall (Score 1 for each correct recall) Question: Can you recall the 3 objects named before?	0-3
5. Language i. Confrontation naming, i.e. naming the objects shown to him. (Score 1 for each correct name) Show him two common objects and ask him to name them (e.g. watch, pen).	0-2
ii. Repetition (Score 1 if repetition is correct verbatim) Ask him to repeat a simple sentence spoken to him (e.g. My country is India).	0-1
iii. Comprehension (Score 1 for each correct step) This is a three stage command. Place a paper on the table and ask him (1) to take the paper with his right hand, (2) fold it in half, and (3) keep it on the floor.	0-3
iv. Reading with comprehension On a paper, write legibly with big letters "close your eyes" and show this to him and ask him to do what it says. Score 1 only if he actually closes his eyes.	0-1
v. Writing spontaneously (Score 1 if he can write correctly) Ask him to write a sentence spontaneously, with a subject and a predicate.	0-1
vi. Copying figures (Score 1 if he copies correctly) On a paper, draw intersecting pentagons each side about 2.5 cm and ask him to copy exactly as it is. See figure.	0-1

and recording the patient's responses. The results are scored numerically and the total score is determined (Table 32.2).

Once the test is completed, find out the total score. The maximum score of 30 is normal. Scores below 15 indicate severe dementia and scores between 15 and 22 indicate moderate-to-mild dementia.

Detailed Mental Status Examination

Record the following points:

Handedness

This refers to preference to use the hand of a particular side, to perform intricate, complex and more skillful motor acts. If a person prefers his right hand to perform these acts, he is labeled as right handed person and if he prefers his left hand, left-handed person. More than 90 to 95% of the general population are right-handed. Hereditary and evolutionary factors, learning during childhood, and cerebral dominance are responsible for the hand preference.

The patient's handedness is determined by asking him which hand he normally uses to comb his hair, lift an object, throw a ball and thread needle.

Educational Status

This should be known because the patient's behavior is heavily influenced by his educational

attainment. Ask him his formal or informal level of education.

Level of Consciousness

Alert/somnolence/stupor/semicoma/coma. Only if the patient is alert further tests are relevant.

Appearance and Behavior

Note whether he is tidy/unkempt/cooperative/indifferent/hostile/agitated/dull.

Affect and Mood

Affect

It is the patient's emotional status, as manifested externally to the examiner. Note whether he is elated/fearful/anxious/apathetic or sad.

Mood

It is the patient's subjective mental state. It must be explored by the examiner.

Orientation

Orientation to Time

Ask him the current day, date, time, month, year and season.

Orientation to Place

Ask him to name the city and hospital he is in.

Orientation to Persons

Ask him to identify the persons, previously known to him.

Attention

It is the ability to attend to a given task. Note the speed and accuracy. Recite a series of digits and ask him to tap on the table when a specific digit is repeated. Note your observations as: attentive/inattentive/distracted/wandering attention.

Comprehension

It is the ability to perceive correctly, interpret, and understand the meaning of sensory stimuli.

Auditory comprehension: First simple and then complex commands are given and the responses noted.

For example: Close your eyes.
Stick out your tongue
Raise your left arm
Close your right eye and touch your nose with the left thumb.

Visual Comprehension

Show him familiar pictures and ask him to identify.

Insight

This refers to the patient's understanding of the situation and attitude towards the general nature, cause and implication of his illness, and his ability to appreciate the need for treatment.

Memory

This is the capacity to retain and recall stored information at will. It consists of:
a. registration, retention and immediate recall
b. recent memory
c. remote memory.

Registration, Retention and Immediate Recall

i. *Digit span test:* Give a series of digits at the rate of the one per second without rhythmic spacing and ask the patient to repeat. Normal person above the age of 14 years should be able to repeat 7 to 8 digits forwards, and 6 digits backwards.
ii. Tell him 3 numbers and names of 3 places and ask him to repeat after 3 minutes, after informing him in advance that he has to remember and recall the items later.
iii. Test the ability to repeat a three-part sentence of several words without error.
iv. Give 4 unrelated words and ask him to recall after 5, 10 and 30 minutes. This tests new learning ability.
v. For non-verbal response, ask him to carry out a three stage motor act on command.
vi. Ask the patient to look at a group of objects placed on a table and then name as many of them as possible from memory without looking at the objects. This is the test for visual memory.

Recent Memory

Ask the patient details about the following:
i. Duration of his hospital stay.
ii. Food items in his last meal.
iii. When, how, and with whom he came to hospital.
iv. Details of the doctors he consulted recently.

v. Significant events of the previous day and week.

Remote Memory

Enquire some of the following as are applicable to the patient.

Date and place of birth and age of the patient.

Name and place of the school he studied. Places of his residence in the past.

Past employment history, date of his marriage, and age at the time of marriage.

Names, ages, and addresses of his siblings. Ask him to recite the alphabets or any song or prayer he learnt in his childhood.

Note: Verify the correctness of the answers with the attendant.

Judgment, Reasoning Power and Abstract Thinking

An appraisal can be made during history taking and examination of various other mental faculties.

Judgment

Ask how the patient would conduct himself in certain hypothetical social situations. For example:

a. When there is a fire in the neighbor's house?
b. When an un-opened letter is found on the road?

Reasoning Power

Ask him to define and differentiate abstract terms, e.g. misery and poverty, lie and mistake, etc.

Test his power to appreciate similarities and dissimilarities. Ask him to detect the similarities and dissimilarities between two fruits (orange and banana), two animals (dog and cat), and two pieces of furniture (table and chair), etc.

Ask him to detect absurdities in a statement as given below:

"I have three brothers Ram, Shyam and me". Abstract thinking: Interpretation of proverbs gives clues to this faculty.

Note: This may be difficult even for some normal persons.

General Knowledge and Information

This depends to a great deal on the educational level, exposure to social environment, and general experience of different situations. Ask him some of the following:

- Names of past and present presidents and prime ministers of India.
- Dates of some of the important national and international events.
- Reports from current newspaper.
- Names of the national holidays and their significance.
- Names of some of States in India and their capitals.
- Names of some important rivers and lakes in the country.

Calculation

The serial subtractions test: Ask the patient to do subtraction of 7 or 3 serially starting from 100. If he fails the test, he should be given simpler additions and subtraction problems. Patients with higher academic achievements should have suitably designed tests.

Interpretation of MMSE

The maximum score is 30. Scores <21 indicate general cognitive impairment.

Language and Speech

Test for the following:

1. Fluency
2. Articulation
3. Prosody
4. Content
5. Naming
6. Repetition
7. Comprehension
8. Reading
9. Writing

Praxis

Praxis is the ability to perform a learned motor activity and apraxia is the inability to do so in the absence of other significant neurological deficits. Use the following items for testing praxis: hammer, scissors, comb, tooth brush.

Extremity Praxis

Three levels of action can be tested using one hand at a time.

First Stage

Subject is asked to demonstrate in pantomime (dumb show) the use of an imaginary object, e.g. pencil, hammer or comb.

Second Stage

The examiner demonstrates a learned movement and the subject is asked to imitate it, e.g. eating.

Third Stage

The patient is given the actual object and asked to demonstrate its use.

Finally test for execution of multistage activity, for example: Taking out a matchbox and lighting a candle in proper sequence.

Praxis in other sites can be tested suitably, for examples: Oro-facial praxis, by asking him do one of the following:

- "Stick out the tongue"
- "Lick the upper lip"
- "Blowing a smoke ring"
- "Coughing out"

Ideomotor Apraxia

This refers to the dissociation of idea of a movement from its execution, though both the idea and ability to execute are intact when tested separately.

First Stage

Patient performs poorly to command. He may not be able to carry out any movement or he may be clumsy, often using body parts as the object.

For example, Pounding the fist or running the fingers through the hair when asked to pantomime the use of a hammer or comb.

Second Stage

Performance improves when he imitates the action of the examiner, though often it still remains imperfect.

Third Stage

Most patients perform normally given the actual object.

Constructional Apraxia

First the patient is asked to draw simple figures like a square, circle or triangle.

Then he is given more complex task and as drawing a 3-D cube, face of clock with time of day, a flower, or a tree.

Look for Dressing Ability

A simple test is to check whether there is mistake performed between the inside and outside of clothes.

Agnosis

Inability to perceive and comprehend the nature of sensory inputs (visual, auditory, or tactile) in the absence of any sensory loss is called agnosis.

Visual agnosis is tested by the following:

Appreciation of color, form, direction and perception of space.

Recognition of fingers and other body parts. Identification of animate and inanimate objects and faces. Color naming and matching.

Auditory agnosis is tested by the recognition of articulated sounds, clicking noise, sound of crumbling paper or a ringing bell.

Tactile agnosia is synonymous with asterio-gnosis. It is the inability to identify shapes and sizes of objects placed on the hand.

SPEECH AND LANGUAGE

In neurological parlance, speech has many more facets to it than what is understood by the lay public. Speech and language are the main modes of expression and communication available to humans. In addition to spoken speech, gestures, signs, signals and graphic symbols of written language all can serve the same purpose. All these modes of expression of thoughts and ideas to others and comprehension of their thoughts and ideas constitute language. Thus, language can be described as the medium of communication. Communication through signs, signals, gestures and vocalizations, mainly to convey one's emotions is called emotional language. Communication through the medium of symbols or words is called symbolic language (spoken and written speech). Infants and to some degree animals, communicate through emotional language. The diencephalon (upper brainstem) and hypothalamus mediate emotional language and it is independent of the cerebral hemispheres. As opposed to this, the symbolic language which is unique to man is dependent on fully mature, intact cerebral functions.

Synthesis of spoken and written language is a function of the brain. This function is lateralized in the left cerebral hemisphere in 99% of right handed and 75% of left handed individuals and it is the dominant hemisphere for speech and language.

Four distinct areas concerned with speech and language are identified in the brain which constitute the cortical areas for speech. Two of these are anterior to the central sulcus and the other two are posterior to it. All the four are located in the perisylvian region which is called the central zone of language. Just as the cortex anterior to the central sulcus is motor and that posterior to it is sensory in function, the two anterior speech areas are responsible for motor aspects of speech, one for spoken speech and the other for visual speech, i.e. writing. The two posterior areas are concerned with the sensory aspects of speech, one for comprehension of spoken speech and the other for comprehension of visual speech, i.e. reading. The motor area for spoken speech, is situated in the posterior part of the left inferior frontal gyrus and it is called Broca's area. The motor center for writing is thought to be just anterior and superior to the Broca's area, very close to that part of the motor cortex that controls the hand muscles. The auditory comprehension of spoken speech takes place in the posterior end of the left superior temporal gyrus (Wernicke's area). The center for reading is thought to be in the medial aspect of the left occipital lobe and the splenium of the corpus callosum. All these speech areas are connected with each other and the rest of the brain by the neural pathways in the underlying white matter.

The conversion of the intended ideas into words and syllables requires synchronized delicate movements involving structures in the larynx, palate, tongue and lips which are supplied by motor cranial nerves. This neuromuscular apparatus constitutes the peripheral mechanism of motor speech, i.e. articulation. Cerebellum coordinates these movements and sounds to produce proper prosodic speech. Defects occurring in specific areas in the central pathways produce characteristic abnormalities. By analysis of the abnormality, the central defect can be inferred.

The role of subcortical gray matter such as the thalamus, and caudate nuclei and the right (nondominant) hemisphere in the total mental and language attainment of humans is being unraveled by modern investigations. It is now realized that all these parts also play major roles.

Complete loss of the spoken speech due to a dysfunction of the central mechanism in the brain is called aphasia, and a minor disturbance is called dysphasia. Loss of ability to read, writing being unaffected is called alexia without agraphia. Loss of ability to write is called agraphia. Dysfunction of the peripheral mechanism of speech leads to defective articulation which is called dysarthria.

Depending on the site of the lesion in the speech areas in the brain, the following types of aphasia may occur (Table 32.3, Fig. 32.1 and Flow chart 32.1).

Examination of Speech and Language

Before proceeding to examine speech, ascertain the following:

i. Handedness of the patient
ii. Language familiar to him for speaking, reading and writing
iii. His general level of education and intelligence

Table 32.3: Types of aphasia based on the site of the lesion in speech areas of brain

Aphasia type	*Site of lesion*
1. Broca's aphasia Syn: expressive, nonfluent, motor or anterior aphasia	Posterior end of left inferior frontal gyrus
2. Wernicke's aphasia Syn: receptive, fluent, Jargon, sensory or posterior aphasia	Posterior end of left superior temporal gyrus
3. Global aphasia	In both the above sites
4. Conduction aphasia	Between the above two sites
5. Transcortical aphasia. a. motor b. sensory	 Anterior and/or superior to Broca's area Posterior and inferior to Wernicke's area.

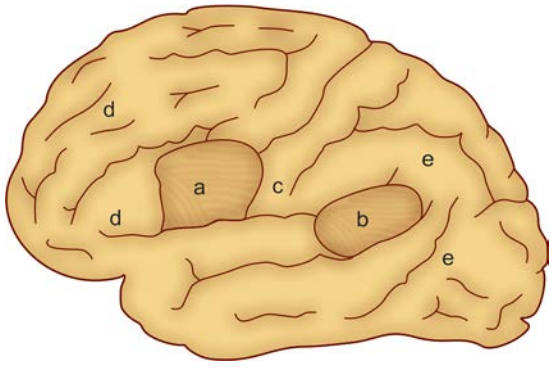


Fig. 32.1: Aphasic syndromes and site of lesion in left cerebral hemisphere

a. Broca
b. Wernicke
c. Conduction
d. Transcortical motor and
e. Transcortical sensory

The level of consciousness, hearing and vision should be sufficiently preserved to administer the tests. Detailed evaluation of speech and language functions is a time-consuming process and it is not usually required for the purpose of localization in clinical neurology. Hence a short and practically useful method of examination is described below.

The patient is assessed for the following:

1. Can he repeat verbatim words or sentences told to him?
2. Can he comprehend the spoken language?
3. How is his spontaneous speech?
4. Can he read, and understand what he reads?
5. Can he write spontaneously, or to dictation, or copy?

Repetition: Tell him names, letters, words or sentences and ask him to repeat verbatim.

Note: Whether he is able to repeat or not.

Comprehension of spoken language: Give a series of verbal commands and note from his responses whether he appears to comprehend them.

These commands should require:

i. Execution of motor acts with the unaffected parts of the body, e.g. show me your tongue, lift your left hand and touch your right eye with your left hand.
ii. Answering questions, e.g. tell me your address, tell me the names of your family members.

Spontaneous Speech

It is the ability to express verbally one's thoughts and ideas.

Ask him to tell about his illness

Show him a picture card or a drawing and ask him to describe the same verbally.

Ask him to recite the days in a week, the months in a year, the alphabets in his language or any song which he knew.

While he is speaking spontaneously, observe the following:

i. *Word output or fluency:* Whether it is normal, reduced, or more than normal. Normal speech is fluent with an average word output of 100 to 150 words per minute.
ii. *Grammar correct or incorrect:* Every language has certain rules of grammar to be followed to convey the desired meaning. Words which convey the meaning are called substantive words and the others which make a sentence grammatically correct (e.g. it, the, on, of, but, etc.) are called fillers. In one type of aphasia the patient may not be able to produce grammatically correct sentences, but by means of substantive words he can convey his ideas or thoughts reasonably well. This is called Broca's aphasia or "telegraphic" speech. On the other hand in Wernicke's aphasia, he cannot convey his ideas and thoughts meaningfully because he uses filler words more than the substantive words. This is called "jargon" speech.

Due to difficulty in retrieving the intended or desired word, the patient puts out a wrong word, e.g. 'She is my husband'. 'You are my medicine', etc. Sometimes he produces a word-like sound which is not existent in the dictionary of any language. Use of wrong words is called "paraphasia" and use of non-existent words is called "neologism".

iii. *Prosody normal or dysprosodic:* Prosody is that quality of speech by which syllables or words are emphasised during spontaneous speech, so as to give it a rhythmic intonation. The rate of speech, the length of the phrases used and the pauses in between these phrases also contribute to the normal prosody of speech.

Disturbances in the prosody of speech may be in the form of either prosodic excess or prosodic insufficiency. The term prosodic excess refers to either unusual prolongation of the pauses between syllables and words or unusually excessive or equal stress on them. Prosodic insufficiency is characterized by reduction in pitch and loudness of the voice, giving it a monotonous quality. However, the rate of speech may be either slow or rapid.

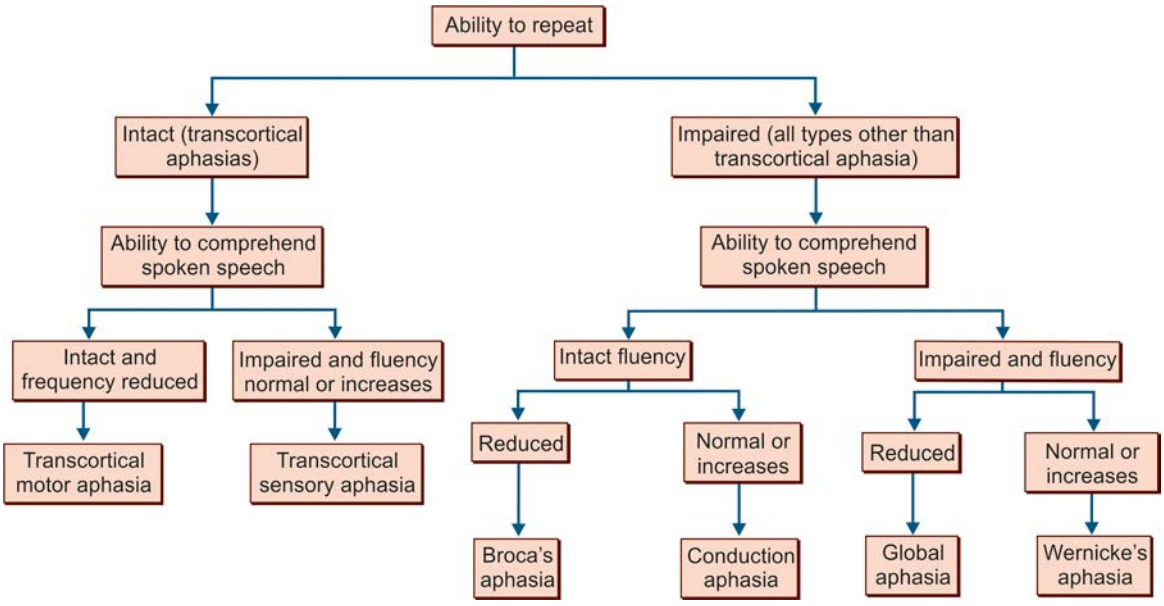
Prosody of speech is observed during conversional speech or it can be tested by asking the patient to repeat certain words, phrases or sentences which contain several syllables in a language familiar to him.

iv. *Confrontation naming:* Show him some common objects and ask him to name them.

Reading

i. *Reading silently with comprehension:* Give him a paper on which a command is written legibly in a language familiar to him and note his response, e.g. tell me your address.

Flow chart 32.1: Scheme of analysis of disorders of speech



ii. *Reading aloud with comprehension:* Give him the same command as above and ask him to read it aloud and respond. A patient may be able to read aloud correctly but he mayor may not comprehend what he is reading.

Writing

Check-up whether the patient was able to write before the onset of the present illness and whether he has any motor deficits which impair his writing.

Then give a paper and pencil and ask him to:

i. Write spontaneously, e.g. about his illness or his address.
ii. Write to dictation.
iii. Copy from a printed page.

After recording the speech and language deficits, they should be analyzed, interpreted and categorized into the appropriate type of aphasic disorder (Tables 32.4 and 32.5). The following algorithm helps to categorize the aphasias.

Table 32.4: Distinction between different types of aphasia

Type of aphasia	*Speech production*	*Speech comprehension*	*Repetition*	*Other features*	*Lesion site*
Broca's	Impaired	Relatively intact	Impaired	Nonfluent, agrammatical, telegraphic, dysarthric, dysprosodic, effortful naming defect	Left inferior (Fig. 32.1) frontal gyrus-posterior part (a)
Wernicke's	Relatively intact	Impaired	Impaired	Fluent, grammatical, jargon, paraphasic, prosodic, effortless, naming defect	Left superior temporal gyrus-posterior part (b)
Global	Impaired	Impaired	Impaired	Nonfluent, agrammatical, naming defect, automatic, emotional speech intact	Lesion at sites (a) and (b)
Conduction	Relatively intact	Relatively intact	Impaired	Fluent, grammatical, paraphasic, confrontation naming defective	Left supramarginal gyrus/or left auditory cortex and insula (c)
Transcortical motor	Impaired	Relatively intact	Normal	Nonfluent, agrammatical	Adjacent to Broca's area (d)
Transcortical sensory	Relatively intact	Impaired	Normal	Fluent, grammatical	Adjacent to Wernicke's area (e)

Table 32.5: Common terms used to describe special forms of dysphasia and the site of lesion responsible for each

Pure word deafness: • Inability to comprehend and repeat spoken language • Relatively preserved written language	Heschl's gyrus and/or its afferent connections
Semantic aphasia: • Inability to comprehend spoken and written language • Normal repetition of spoken language	Parietotemporal border zone Angular gyrus and its connections to posterior inferior temporal cortex
Aphasic anomia: • (Syn: word finding difficulty, nominal aphasia) • Word production anomia: • Inability to produce correct words, but does so on prompting	Broca's area and its connections
Word selection anomia: • Inability to produce correct word even on prompting, but can select the word if choice is given	Left second temporal gyrus-posterior part of temporo-occipital junction.
Semantic anomia: • Inability to select the correct word even if the same is offered	Left angular gyrus
Alexia with agraphia: • Reading difficulty and writing difficulty	Left angular gyrus
Alexia without agraphia: • Reading difficulty with normal writing (pure word blindness)	Medial part of occipital lobe and splenium of corpus callosum
Alexia for syntax: • Inability to comprehend the meaning of a series of words in a sentence that he is able to read, although he can read and comprehend individual words	Broca's area
Agraphia: • Inability to write	Left angular gyrus/left second frontal gyrus

Associated Motor Deficits often seen along with these Aphasias

Weakness of right side of face, and right arm with Broca's aphasia. No weakness with Wernicke's aphasia. Weakness of right half of body with global aphasia.

Speech Articulation

Articulation is the process of production of syllables by the coordinated action of facial, lingual and palatal muscles controlled by the cerebellum.

Precise rate, range and strength of movements of these muscles are necessary for normal speech. Alteration in any of these aspects of motor speech resulting from a neurological disorder leads to dysarthria. Depending on the nature of the underlying neurological disorder, the pattern of dysarthria varies (Table 32.6). Dysarthria may be spastic, flaccid, ataxic, hypokinetic, hyperkinetic or mixed in type (Table 32.7).

Testing: A preliminary appraisal can be made during interrogation. Further information can be obtained by detailed examination. The patient is asked to repeat sentences containing words comprising of several syllables.

Phonation

Phonation is the process by which voice is produced by the vocal cords. Disturbance of phonation gives rise to dysphonia.

Testing: The patient is asked to repeat as rapidly and regularly as possible syllables or words which involve specifically the movements of the lips and tongue, such as puh, tub, kuh, etc. The rate, rhythm and range of the movements are noted.

Spasm of adductor muscles of vocal cords results in a voice which is strained, harsh and low pitched.

Nasality of Voice

The normal resonance of voice is dependent on normal oropharynx, nasopharynx and the communication between these two structures. Local lesions in oropharynx and nasopharynx will result in hyponasality of voice due to obstruction to airway. Weakness or paralysis of the soft palate, resulting in partial closure or nonclosure of the communication between naso and oropharynx will produce hypernasality of voice.

Nasality of voice is tested during conversational or contextural speech. Normal phonation,

Table 32.6: Clinical features and causes of common dysarthrias and other speech defects

Type	Features	Disease
A. Due to lesions in the central nervous system:		
a. Slurred speech	Individual letters are slurred, precision of consonant pronunciation is lost as in a state of intoxication	Diffuse cerebral disease
b. Scanning speech	Speech is slow, and the syllables in a word are pronounced clearly with unduly prolonged pauses in between	Cerebellar disease
c. Staccato speech	Intermittent, jerky and explosive pronounciation of some syllables	Cerebellar disease
d. Monotonous speech	Low pitched voice lacking in melodic intonations	Parkinsonism
e. Hiccup speech	Abrupt interruption in the pronounciation of words or abrupt jerky pronounciation of words	Chorea, myoclonus
f. Cortical dysarthria (spastic speech)	Slow, thick and indistinct speech	Lesion in left frontal cortex and recovering phase of Broca's aphasia
B. Due to lesions in the peripheral nervous system		
a. Slurred	Difficulty in pronounciation of vibratives (R) lingual and labial consonants (P,L,M) making the speech indistinct	Bulbar palsy myopathy myasthenia gravis
b. Dysphonia	Low pitched voice	Bulbar palsy
c. Hoarse voice	Low pitched, rough, harsh voice	Laryngeal palsy
C. Of undetermined cause		
a. Stammering	Repetition of syllables in a word	
b. Stuttering	Repetition of syllables in a word usually only at the commencement of the word	

Table 32.7: Features of different types of dysarthria

Dysarthria type	Phonation	Prosody	Nasality	Pitch	Loudness	Rate	Disease
Spastic	Strained voice, tremor	Excess or insufficient	Hyper or hypo	Low or monotonous	Harsh or monotonous	Slow	Pseudobulbar palsy
Flaccid	Impaired	Insufficient	Hyper	Low	Reduced	Slow	Bulbar palsy
Spastic and Flaccid	Strained	Excess or insufficient	Hyper	Low	Hoarse	Slow	Amyotrophic lateral sclerosis
Ataxic	Strained	Excess	Normal	Irregular	Irregular	Slow	Cerebellar disease
Hypokinetic	Difficulty in initiation of speech	Insufficient	Normal	Reduced monotonous	Reduced monotonous	Slow	Parkinsonism
Hyperkinetic	Strained	Unpredictable variations	Normal or hypo	Reduced monotonous	Unpredictable excessive variations	Variable	Dystonia

prosody and nasality of voice depend on adequate respiratory airflow. In conditions with low vital capacity, all the modalities tend to be abnormal.

CRANIAL NERVES

General Considerations

There are 12 pairs of cranial nerves which leave or enter the brain through foramina at the base of the skull. All these nerves supply different structures in the head and neck. The tenth nerve also supplies the viscera in the thorax and abdomen. The olfactory, optic and vestibulo-cochlear nerves are purely sensory nerves. The oculomotor, trochlear, abducent, spinal accessory and hypoglossal nerves are purely motor nerves. The trigeminal, facial, glossopharyngeal and vagus nerves contain both sensory and motor components. The nuclei of the motor cranial nerves (lower motor neurons—LMN) receive impulses from the motor cortex through corticonuclear or corticobulbar fibers (upper motor neuron fibers—UMN). Bilateral UMN connections are present for all the motor cranial nuclei except that part of the facial nucleus which supplies the muscles of the lower part of the face and that part of the hypoglossal nucleus which supplies the genioglossus muscle.

The sensory afferents of the cranial nerves are formed by the axons of the nerve cells situated in the ganglia on the nerve trunks or from sensory organs such as nasal mucosa, retina or internal ear. These form the first order neurons. Their central processes terminate on the cells in the brainstem which form the second order neurons. The axons of the second

order neurons cross the midline and ascend to other sensory nuclei such as the thalamus where they synapse with the third order neurons. The axons of the third order neurons terminate in the sensory cortex of the cerebrum.

Systematic examination of the cranial nerves is an important component of neurological examination.

OLFACTORY NERVE—I CRANIAL NERVE

The olfactory mucous membrane in the upper part of the nasal cavity contains olfactory receptors. The central processes of these receptors form the olfactory nerve fibers which pass through the openings of the cribriform plate of the ethmoid bone and synapse with specialized cells in the olfactory bulb. The central processes of the cells in the olfactory bulb form the olfactory tract which travels posteriorly to reach the anterior perforated substance. Here it divides into medial and lateral olfactory striae. The medial olfactory stria connects the olfactory bulb of one side with that of the opposite side. The lateral olfactory stria carries the fibers to the primary olfactory cortex situated in the periamygdaloid and prepyriform areas of the temporal lobe. The primary olfactory cortex has connections with the secondary olfactory cortex in the parahippocampal gyrus of the temporal lobe and also with many other areas in the brain. These subserve emotional and autonomic responses resulting from olfactory sensations.

Test

Local causes which impair the sense of smell like rhinitis, sinusitis and gross deviation of nasal septum should be looked for and excluded before testing the smell. Each nostril is tested separately after occluding the other one, by using substances with mild aroma like coffee powder, soap, talcum powder, clove or peppermint oil. The patient is asked to close his eyes and mouth and inhale the odor of test substance and indentify it. Ability to perceive the smell and differentiate one smell from the other is taken as normal, even though proper identification may not be possible. Substances which give pungent smell such as ammonia, should not be used because they may stimulate the trigeminal nerve endings and irritate the nose, even when the sense of smell is absent.

Abnormalities of the sense of smell include inability to perceive smell (anosmia), and perversion of smell (parosmia).

Anosmia occurs due to lesions in the olfactory bulb or tract. Fracture of the floor of the anterior cranial fossa, tumors of the olfactory bulb such as olfactory groove meningioma, frontal lobe tumors pressing on the olfactory pathways or basal meningitis may lead to anosmia. Parosmia occurs following head injury.

Since the olfactory tracts on both sides are interconnected through the anterior commissure, unilateral lesions of olfactory cortex do not result in anosmia.

OPTIC NERVE—II CRANIAL NERVE

(Also Refer to Section 17—Ophthalmology)

The optic nerve is the sensory nerve concerned with vision. Rods and cones in the retina are the visual receptors. Rods mediate vision in the dark whereas cones are for vision in brightness. Macula situated at about the center of the retina contains more cones than rods and it is responsible for the clearest central vision. Fovea which contains only cones is responsible for color vision and central vision. The remaining portions of the retina contain more rods than cones. They take part in peripheral vision, perception of movement of objects in the visual field and vision in darkness, but not for color vision. The fibers of the optic nerve are the axons of the ganglionic cells in the retina which are connected to the rods and cones through intermediate neurons. The nerve fibers converge on the optic disk and exit posteriorly to form the optic nerve. Optic nerve head (optic disk) produces the physiological blind spot in the visual field, being devoid of rods and cones. The blind spot lies on the temporal side of the point of visual fixation, slightly below the horizontal meridian of the visual field. Fibers of the optic nerve have central type of myelin sheath. The myelin sheath stops short at the lamina cribrosa. The dura, arachnoid and pia mater extend forward around the optic nerve up to the lamina cribrosa. The subdural and subarachnoid spaces around the optic nerve are in direct communication with those around the brain. Optic nerve leaves the orbital cavity through the optic foramen and unites with the optic nerve of the opposite side to form the optic chiasma. In the

chiasma the fibers from the nasal half of each retina including that of the macula cross the midline, pass anteriorly for a short distance into the opposite optic nerve and then pass posteriorly to enter the optic tract. The fibers from the temporal half of each retina including that of the macula do not cross. They pass in the optic tract of the same side.

Position of the optic chiasma may vary within small limits even in healthy individuals. The optic chiasma lies directly above the sella turcica, if the optic nerves are short, but more commonly it lies slightly behind and above the sella turcica. Due to this anatomical variation the visual field defects caused by pituitary tumors may vary in different patients.

The optic tracts pass posterolaterally around the lateral surface of the cerebral peduncles of the midbrain. All the fibers of the optic tract concerned with visual perception terminate by synapsing with cells in the lateral geniculate body. Fibers that are concerned with pupillary light reflex pass to the pretectal nucleus and the superior colliculus of the midbrain.

Course of the Visual Perception Fibers

The lateral geniculate body is a projection from the pulvinar of the thalamus and the axons of the nerve cells from here proceed to form the optic radiation. The fibers in the optic radiation fan out in the parietal, temporal and occipital lobes of the cerebral hemisphere, and reach the visual cortex on the medial side of the occipital lobe. The fibers in the parietal lobe carry visual information from the lower half of the visual field and those in the temporal lobe carry visual information from the upper half of the visual field. In their course, the fibers in the optic radiation (optic peduncle) are in close relation to the posterior limb of the internal capsule. The primary visual cortex (area 17 or striate cortex) lies on either side of the calcarine fissure. In the visual cortex neurons in the anterior 1/3 are responsible for peripheral vision, neurons in the posterior 1/3 are responsible for central vision and neurons at the tip are responsible for macular vision. The upper field of vision projects to the lower side and the lower field to the upper side of the calcarine fissure. The primary visual cortex is surrounded by visual association cortex (area 18 or parastriate cortex and area 19 or peristriate cortex), which is responsible for visual localization and discrimination, spinal orientation and complex visual perceptions.

There is a definite topographical arrangement of the retinal fibers in the visual pathways. Fibers from the upper part of the retina occupy the upper part of the optic nerve and those from the lower part of the retina occupy the lower part of the nerve. The macular fibers occupy a central position. In the optic chiasma, optic tract and optic radiation, the fibers from the upper part of the retina occupy the upper or dorsal position, and the fibers from the lower half of the retina occupy a lower or ventral position.

Tests of function: The following features must always be examined:

i. Visual acuity, ii. Visual fields,
iii. Color vision, and iv. Optic fundi.

Note: Each eye should be tested separately by covering the other one. Local causes of visual impairment such as refractory errors and opacities in the media have to be excluded before attributing visual impairment to a neurological lesion.

Visual Acuity

Visual acuity is the resolving power of the eye for central vision, both for near as well as distant objects in the visual space. It should be assessed in both eyes separately. Near as well as distant vision should be tested because some neurological and ocular diseases affect these two types of vision disproportionately. If the patient is wearing glasses, his vision should be tested both with and without glasses.

Near Vision

It is tested by asking the patient to read letters of different sizes printed on a reading card (American Medical Association reading card or Jaeger's test chart). The reading card is held at 35 cm from the patient's eye and the smallest line which can be read is determined. A person with normal near vision, can read the line of letters designated '14' and the visual acuity is recorded as '14/4'. This method is particularly useful in neurological practice since it can be employed even in bed-ridden patients. Patients with presbyopia should

wear their reading glasses when their visual acuity is tested. Alternatively, the patient can be asked to read an ordinary newsprint or identify small pictures on a card held at 30 to 35 cm from his eye.

Distant Vision

The standard clinical test for distant vision is Snellen's test. The Snellen's chart contains letters of various sizes, arranged in horizontal lines. The number beside each line indicates the distance in feet, at which the letters can be read by a person with normal vision. Snellen's chart is kept at a standard distance of 6 meters (20 feet) from the patient's eyes. At this distance, ocular accommodation does not occur and the light rays will be parallel. Normally, the smallest letters in the line designated "6" can be read at 6 m and then the visual acuity for distant vision is recorded as 6/6. If distant vision is affected, the patient can read only larger letter types, in which case, the visual acuity is recorded as '6/x', 'x' being the number designated to the smallest line the patient could read.

Modified Snellen's charts with vernacular letters, numbers, symbols or pictures are available for those who are not able to read English letters.

If a patient cannot read any letter on the Snellen's chart, even when standing near it, visual acuity is tested by noting the ability to count fingers (CF), ability to appreciate the movements of the examiner's hand (EH), or ability to perceive light (PL). With increasing degrees of visual loss, these faculties disappear progressively. When the patient cannot even perceive light, the vision is recorded as "no PL". Projection of light is the ability to know the direction from which the light is entering the eye.

For patients who are disabled and bedridden, a quick method is to find out the ability to count fingers correctly at various distances. Finger-counting at 3 m is approximately equal to visual acuity of 6/60 on Snellen's test.

Pin-Hole Test

The patient is asked to look at an object through a 1 mm size pin hole, punched in a card. The pin-hole allows the light to fall only in the central part of the retina. *If the visual acuity which is originally impaired improves on pin hole test, the visual impairment is due to refractive error and not due to any neurological cause.*

Other local ocular conditions such as cataract, glaucoma, and opacities in the media are also common causes of visual impairment.

Patterns of onset of visual impairment in neurological disorders:

i. **Sudden, transient, monocular blindness,** coming on like a curtain falling swiftly over the upper half of visual field and lasting for 5 to 15 minutes should suggest embolism of central retinal artery. This is called "amaurosis fugax". It may persist for a longer time if it leads to retinal infarction. Visual loss occurring at the onset of calssical migraine may also follow a similar pattern. It is due to vasospasm.

ii. **Severe visual loss in one eye** usually developing over a few hours or even a day or two to reach its peak, occurs in optic neuritis or ischemic optic neuropathy. Patient with hypertension, diabetes, atherosclerosis, collagen vascular disease or temporal arteritis are more prone to develop vascular occlusion.

iii. **Brief, transient, hazy obscurations of vision** lasting for less than 10 seconds in one or both eyes occur characteristically in patients with severe papilledema caused by raised intracranial pressure. In the later stages progressive diminution of vision develops.

iv. **Insidious and progressive visual loss in one eye** may result from a tumor such as optic nerve glioma compressing the optic nerve either in the orbit or optic foramen.

v. **Insidious and progressive visual loss affecting both eyes** is the hallmark of compression of the optic chiasma by tumors. Toxic, nutritional, and metabolic causes and hereditary optic atrophies also lead to such a progressive visual loss.

Visual Fields

Visual field is the visual space in front of the eye in which objects are visible when the eye is fixed in one direction. In each eye the normal visual field extends up to 100° on the temporal side, 60° on the nasal and upper side, and 70° on the lower side. The visual field extending up to 30° from the point of ocular fixation is called central field and the rest is called peripheral field. During binocular vision, the visual fields of both eyes overlap except over a crescent shaped area at the periphery of the temporal field of each eye which is perceived only

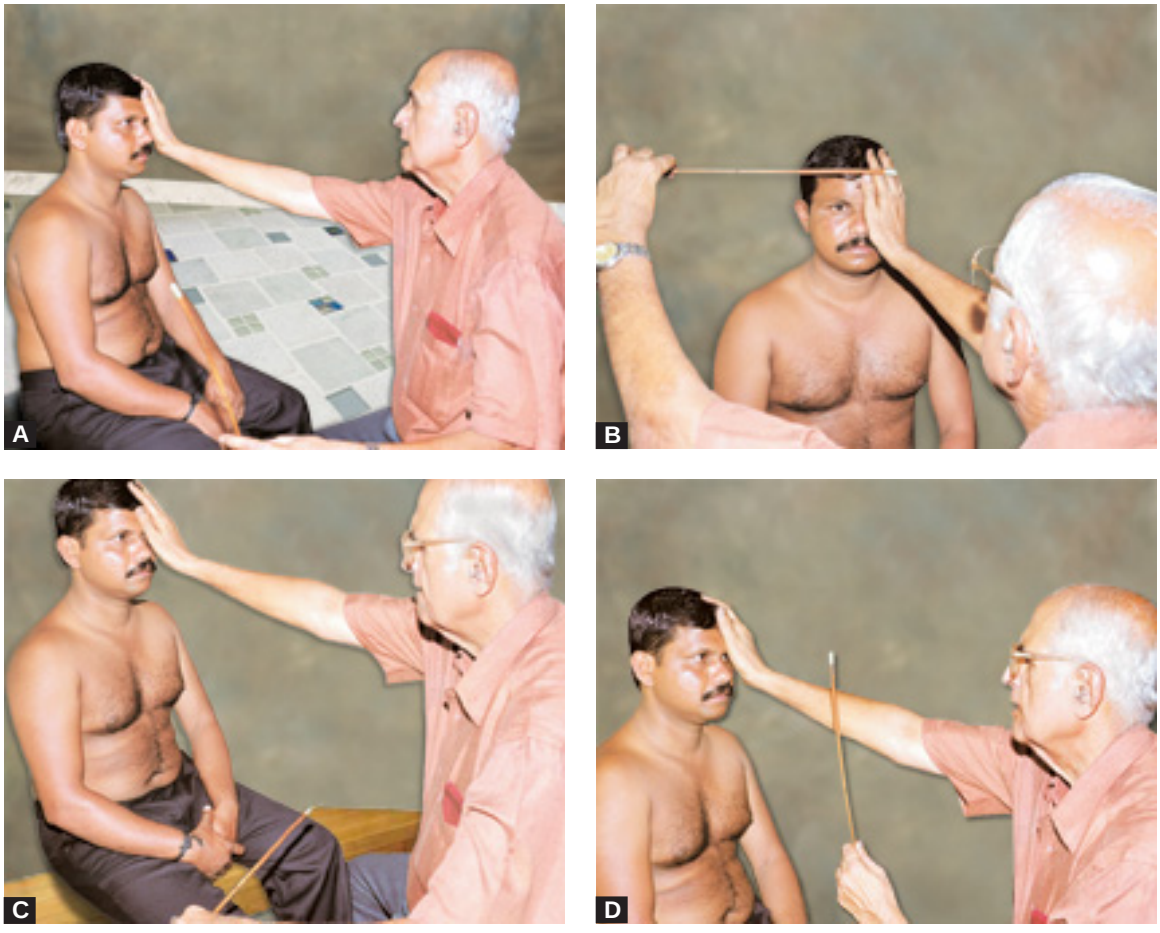
by the ipsilateral eye. Damage to the visual pathway at any point from the retina to the visual cortex can result in an abnormality in the visual fields. The pattern of such a visual field defect helps to localize the lesion.

Tests: Visual field can be assessed at the bedside by confrontation method. It can also be precisely charted using a perimeter or Bjerrum's screen.

Assessment of Peripheral Fields of Vision (Figs 32.2A to D)

Confrontation Method

In this method the visual fields of the patient are compared with the visual fields of the examiner which have to be normal. The examiner positions himself face to face in front of the patient at 60 to 75 cm distance in such a way that his eyes and the eyes of the patient are almost at the same level. Each eye is tested separately, while the other eye is covered. For testing the right eye of the patient he fixes his eye on to the left eye of the examiner and vice versa. Throughout the examination, the patient and the examiner should not change the position of their eyes. The examiner should bring a moving object such as his finger, pen or preferably a white pinhead from the periphery towards the point of fixation, keeping the moving object midway between the patient's eye and the examiner's eye, the upper nasal, lower nasal, upper temporal and lower temporal quadrants are tested individually. The patient is asked to indicate by saying 'yes' or raising his hand, as soon as he sees the object. By comparing with his own visual field, the examiner



Figs 32.2A to D: Confrontation method for testing field of vision: (A) Lateral (temporal) field (*See* text for description), (B) Upper field, (C) Lower field, (D) Medial (nasal) field

can detect gross defects in the patient's visual field. This method detects the outline of the visual field.

A less accurate method is to test the ability to count the fingers of the examiner in each quadrant of the visual field. While examining patients who are less cooperative or demented, and in children, a small shiny or colorful object can be brought into the visual field from the periphery in each quadrant and the response of the patient noted. Turning the eyes and head in the direction of the object may give clue to normal visual function.

When standard procedures are not applicable as in totally bedridden patients, uncooperative children, or demented subjects the defensive blinking response brought about by moving the examiner's hand rapidly from the periphery towards the patient's eye can be tested. Absence of expected response should suggest loss of vision in the part of the visual field.

Visual inattention is also tested by confrontation tests by keeping both eyes open. After testing the visual fields in each eye separately, two identical stimuli (e.g. index fingers of the examiner) are presented simultaneously in corresponding positions of both visual fields. If visual inattention is present the patient appreciates the finger only on one side although the visual fields are normal in both eyes when tested separately.

Assessment of Central Field of Vision

Central visual field can be assessed by the red-pin test. Since the central portion of the retina is rich in cones which are the only color-sensitive receptors, a red-pin is used as for the confrontation test. As in peripheral field of vision, the red-pin is brought from the periphery towards the center in all quadrants and the patient is asked to compare the sharpness and brightness of the object in each position. Scotomas can be detected by this method.

Macula is responsible for central vision that extends up to 5° from the center of the visual field. In occipital lobe lesions, this macular vision may be spared even in the presence of hemianopia. Alternatively, macular vision alone may be affected.

Preservation of macular vision in the presence of hemianopia can be detected by charting the visual field using the red-pin.

Detection of Blind Spot

The physiological blind spot is situated on the temporal side of the central point of fixation. It can be detected by the red-pin test. Its size should coincide with the examiner's blind spot. More reliable method is to do perimetry.

Note: I. Confrontation method is partly subjective and it detects only gross defects in the peripheral field of vision.

II. The visual field is larger when the test is done with (1) larger objects, (2) moving objects, and (3) white color objects instead of other colors.

Types of Visual Field Defects

i. *Hemianopia (Syn: hemianopsia):* Loss of one half of visual field.

- *Homonymous hemianopia:* Loss of vision in the nasal half of one eye and temporal half of the other eye, i.e. loss of the right or left field of vision.
- *Congruous hemianopia:* The contour of outline of the visual loss in the homonymous fields of the two eyes is similar because of relative compactness of visual fibers in optic tract and lateral geniculate body.
- *Incongruous hemianopia:* The contour of the visual loss in the homonymous fields of the two eyes is dissimilar because of relative separation of visual fibers as in the optic radiation.
- *Macular sparing:* Homonymous visual field defect in which the macular vision is preserved.
- *Heteronymous hemianopia:* Loss of vision in the nasal halves or temporal halves of both eyes, i.e. binasal or bitemporal defects.

ii. *Quadrantanopia:* Loss of vision in one quadrant of the visual field in one or both eyes, i.e. upper nasal, lower nasal, upper temporal or lower temporal.

- In homonymous quadrantanopia, corresponding quadrants may be lost in each visual field, e.g. upper temporal quadrant of one eye and upper nasal quadrant of the other eye or lower temporal quadrant of one eye and lower nasal quadrant of the other eye. Quadrantanopia may be heteronymous, i.e. the same quadrant in both eyes may be affected, e.g. bilateral

upper nasal, bilateral upper temporal, bilateral lower nasal and bilateral lower temporal.

iii. *Altitudinal hemianopia:* Loss of vision in the upper or lower half of visual field in one or both eyes.

iv. *Concentric constriction:* Loss of vision at the periphery of the visual field, often progressing in a concentric fashion.

Scotoma

This is an area of defective vision in the visual field. Total blindness in the area is termed 'absolute scotoma' and partial visual loss is called 'relative' scotoma. If the patient is aware of the defect such a scotoma is called 'positive' scotoma. 'Negative' scotoma is one which is not appreciated by the patient, but detected by the examiner. 'Subjective' scotoma is one which is felt by the patient, but not detectable on examination. This may take the form of scintillating scotomas or fortification spectra, i.e. bright colorless or colored flashes of light. 'Objective' scotoma is the one that can be demonstrated by examination. Scotoma may take several forms around the point of fixation. Scotomas adjacent to the point of fixation are called 'paracentral' scotomas. 'Cecocentral' scotoma is one which extends from the point of fixation to the normal blind spot. 'Ring' scotoma (annular scotoma) is one that encircles the point of fixation.

Tubular contraction of visual field: In this condition the visual field is constricted as if the patient looks through a tube without the normal expansion of the field of vision as the patient looks at objects farther away. In tubular contraction, the visual field remains constant. It is usually a sign of hysteria, but rarely it can occur in frontal lobe lesions, and conditions like retinitis pigmentosa.

Spiral contraction: When the visual field is tested repeatedly at the same sitting, it constricts progressively with each test. Usually this suggests a hysterical phenomenon. Sometimes it can occur due to fatigue. Rarely it may be due to a frontal lobe lesion.

Star-shaped field: The outline of the visual field is uneven with multiple projection like a star. It has the same significance as spiral contraction.

Site of Lesion in Visual Pathway and the Resultant Visual Field Defects (Figs 32.3A and B)

Optic Nerve

A complete lesion such as optic nerve injury produces total blindness in the eye. Conditions such as optic neuritis and compression of the optic nerve result in incomplete lesion which gives rise to central scotomas in the affected eye. Bilateral central scotomas occur in optic neuropathies. If the lesion is in the posterior most part of the optic nerve close to the optic chiasma, loss of vision in the ipsilateral eye and contralateral upper temporal quadrantanopia may develop. Optic neuritis, optic atrophy, trauma, tumor and ischemia are the common lesions which affect the optic nerve.

Swinging flash test: Normally when the pupils on both sides are rapidly and alternately stimulated by swinging a torch light, both pupils tend to remain constricted. But if there is a lesion in one optic nerve, the pupils will dilate when the light is transferred to the affected side, while on transferring the light rapidly to the normal side, both pupils will constrict. This is also called the Marcus Gunn pupil. It is an early sign of optic nerve disease such as optic neuritis.

Optic Chiasma

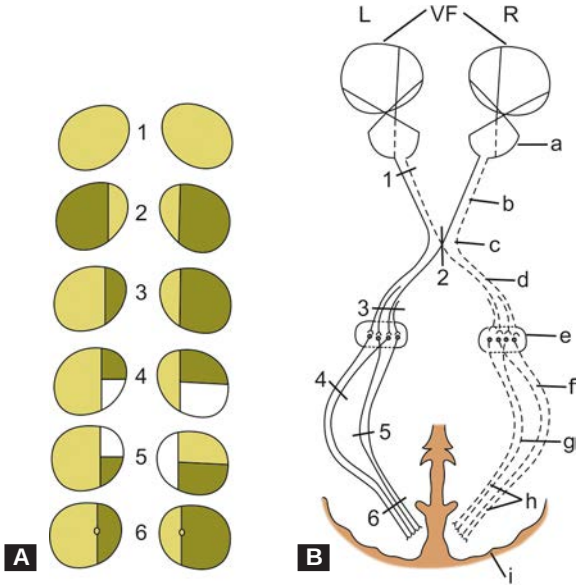
i. Central portion: Bilateral hemianopia is the classic finding.
 - *Causes:* Pituitary tumor, craniopharyngioma, hydrocephalus, tumor in third ventricle, other space occupying lesions in the sellar and suprasellar region and arachnoiditis affecting the chiasma.

ii. Lateral portion on one side: This leads to ipsilateral nasal hemianopia.
 - *Causes:* Atherosclerotic carotid artery aneurysm pressing upon this part of the chiasma.

iii. Lateral portion on both sides: Binasal hemianopia develops.
 - *Causes:* Atherosclerotic tortuous carotid arteries in elderly subjects; bilateral carotid artery aneurysms in the parasellar regions.

Optic Tract

Lesions result in congruous homonymous hemianopia on the contralateral side.



Figs 32.3A and B: (A) Visual field defects, (B) Visual pathways

A. Visual field defects:
1. Left eye blind—lesion in optic nerve
2. Bitemporal hemianopia lesion in central part of optic chiasma
3. Right homonymous hemianopia with macular splitting lesion left optic tract
4. Right upper quadrantanopia—lesion optic radiation passing through left temporal lobe
5. Right lower quadrantanopia—lesion optic radiation passing though anterior part of left parietal lobe
6. Right homonymous hemianopia with macular sparing

B. Visual pathway and sites of lesions:
a. Retina
b. Optic nerve
c. Optic chiasma
d. Optic tract
e. Lateral geniculate body
f. Optic radiation, lower fibers in temporal lobe
g. Optic radiation, upper fibers in anterior parietal lobe
h. Posterior parietal lobe, all fibers of optic radiation
i. Occipital cortex

Causes

Compression by tumors and other space occupying lesions, demyelination.

Lateral Geniculate Body

Visual field defects resemble those of optic tract lesion.

Causes: Compression by tumors or other space occupying lesions affecting this region.

Optic Radiation

Homonymous hemianopia on the contralateral side.

a. *Temporal lobe:* Incongruous homonymous, upper quadrant anopia on the contralateral side.
b. *Parietal lobe:* Incongruous homonymous, lower quadrantanopia on the contralateral side.
c. *Occipital lobe:* Incongruous homonymous hemianopia on the contralateral side. Macular sparing may or may not be present.

Occipital Cortex

Congruous homonymous hemianopia on the contralateral side with sparing of macular vision.

Note: 1. A complete homonymous hemianopia with clear-cut demarcation between the defective and normal field should suggest a vascular cause. A partial field defect which has less distinct margins and which becomes larger as the object size is reduced is suggestive of a space occupying lesions in the cerebral hemisphere. The visual defect, in this case enlarges progressively with time.
2. Concentric constriction of visual field occurs in papilledema, bilateral lesions of visual cortex, retinal lesions like retinitis pigmentosa and hysteria.
3. Bilateral hemianopia may be due to lesions in both occipital lobes such as trauma infarction or cortical vein thrombosis. These are rare.

4. Normal visual acuity with preservation of light reflex and no signs of optic atrophy in the presence of homonymous hemianopia suggests a lesion beyond the lateral geniculate body. In lesions anterior to the lateral geniculate body, the visual acuity will be reduced, light reflex will be absent and there may be associated optic atrophy.

Visual Disturbances Caused by Lesions in the Cerebral Cortex

A variety of subjective visual sensation or disturbances occur with or without defects in visual acuity and visual fields as a result of cortical or subcortical lesions. Some of these are given in Table 32.8.

Color Vision

Normal eye can identify and differentiate different shades of color. Three types of cones present in the central region of the retina are responsible for color vision. Color vision has to be tested in bright day light. Discrimination between primary colors such as red, blue and green or combination of colors such as yellow, violet or orange is to be tested.

Test for color vision: Each eye is tested separately for the three primary colors, i.e. red, blue and green and their combinations. A simple test is to show objects or pictures of different colors and ask the patient to identify their color. A more sensitive test is Ishihara's pseudoiso-chromatic test. In this test, test cards, containing dots of various hues but of similar brightness are arranged in such a way that a person with normal vision can identify a figure or figures from the background, whereas a person with defective color vision makes mistakes in correct identification. However, with Ishihara's test cards, only red and green colors can be tested. For testing other colors, other similar test materials are available.

Clinical Importance of Color Blindness

Defective color vision may be an inherited or acquired disorder. Common abnormality in color vision is red-green deficiency which is a sex linked recessive trait. Blue-yellow deficiency may occur as a rare congenital disorder. Lesions of the visual cortex may result in color blindness. In hysterical conversion reaction, color blindness is a common symptom. Color vision is impaired earlier in optic nerve lesions that retinal lesions. Retinal diseases affect blue color first and green last; whereas lesions in the optic pathway affect red and green colors first. The exceptions are ischemic optic neuropathy and autosomal dominant inherited optic atrophies. Normal color vision with grossly reduced visual acuity suggests that the visual loss is not of neurologic cause. If a colored object appears less bright when viewed with one eye as compared to the other, a lesion of the optic nerve should be considered, if an ophthalmological cause is excluded.

Pathways for the Pupillary Reflexes

When a beam of light is thrown into one eye, normally both the pupils constrict. The constriction on the same side is called 'direct' light reflex. The simultaneous constriction of the other pupil is called the 'consensual' light reflex.

The afferent pathway for this reflex is through the optic nerve, optic chiasma and optic tract. In the optic tract, a small number of nerve fibers separate out to synapse on the neurons in the pretectal nucleus which lies close to the superior colliculus in the midbrain. The impulses are then passed by the axons of the pretectal neurons to the parasympathetic nuclei (Edinger-Westphal nuclei) of the third cranial nerve of both sides, where they synapse. The parasympathetic nerve fibers pass through the third cranial nerve to the ciliary ganglion in the orbit. The postganglionic parasympathetic fibers from the ciliary ganglion pass through the short ciliary nerves to the eye to innervate the constrictor pupillae muscle of the iris and ciliary muscles. The fact that the pretectal nucleus has connections with the Edinger-Westphal nuclei of both sides accounts for the consensual light reflex.

Pathway for Accommodation Reflex

When the gaze is shifted from a distant object to a near object, both medial recti contract and the eyes converge. The ciliary muscles contract and this leads to increase in thickness of the lens and thereby its refractive power increases. In addition, both pupils constrict in order to restrict the light

Table 32.8: Visual disturbances caused by cortical lesions

Symptom	*Description*	*Site of lesion*
1. Visual hallucinations	Subjective feeling of visual images in the absence of visual stimulus	
a. Unformed hallucinations	Scintillations and fortification spectra	Irritative lesions of occipital lobe, migrainous headache, or occipital lobe seizures
b. Formed hallucinations	Images of real objects	Irritative lesions of temporal lobe and temporal lobe seizures
2. Defective perception of form	Images of objects appear distorted-too big (macropsia), too small (micropsia), too distant (teleopsia) and other similar disturbances	Posterior occipital or temporal lobe lesions
3. Defective perception of color	The objects appear only as black and white (achromatopsia) or of some other color (dyschromatopsia)	Bilateral occipital lobe lesions on their inferior surface
4. Cerebral diplopia and polyopia	A type of visual illusion in which instead of one, patient sees two or more images of an object	Posterior cerebral hemisphere lesion, the exact site not known
5. Palinopsia	A form of visual perseveration in which visual images persist or reappear for some time even after the visual stimulus is removed	Posterior cerebral hemispheric lesions, the exact site not known
6. Color agnosia	Patient can perceive the colors but cannot name them correctly	Lesion in the splenium of the corpus callosum
7. Visual agnosia	Patient cannot recognize objects visually even though vision is normal	Parieto-occipital lesions
8. Prosopagnosia	Inability to recognize familiar faces	Bilateral occipital or occipitotemporal lesions on their inferior surface
9. Visual disorientation	Inability to localize objects placed in the visual field and inability to gauge the direction, distance or relative positions of objects in space	Bilateral, posterior occipitoparietal lesions
10. Simultanagnosia	Inability to perceive the whole object from its individual components, e.g. when shown a picture, the patient can describe individual features but not the picture as a whole. Similarly, when asked to read, he can do so only by spelling the words letter by letter	Disconnection of occipital cortex from parietal lobe
11. Visual inattention	Inability to perceive one of two visual stimuli, when two identical stimuli are simultaneously applied in both visual fields symmetrically	
12. Denial of blindness	Patient is unaware that he is blind and stoutly denies the fact when brought to his notice	Lesion in the central connections of striate cortex on both sides

rays entering the eyes. All the three components occurring simultaneously constitute the accommodation reflex.

The afferent pathway travels in the visual pathway reaching the occipital cortex (visual cortex). The visual cortex on either side is connected to the frontal eye fields from where the efferent corticomesencephalic fibers descend through the internal capsule to reach the oculomotor nuclei. Some fibers from the oculomotor nuclei reach the medial recti muscles. Some of the descending fibers synapse with the Edinger-Westphal nuclei on both sides from where fibers reach the constrictor pupillae and ciliary muscles (*see* pathway for light reflex). Accommodation brought on by a visual stimulus is mediated through this pathway.

Normal persons can also accommodate for near vision voluntarily even without visual stimuli. This response is mediated through the frontomesencephalic pathway.

Fundus Examination—Funduscopy

(See Chapter 48) Funduscopy is the examination of the interior of the eyes using the ophthalmoscope. For best results the optic fundus is examined in a

dark room. Hold the ophthalmoscope in your right hand, and use your right eye to examine the patient's right eye and vice versa for examining the left eye. Ask the patient to fix his vision at any distant object at eye level and then keep the eyes still. Focus the ophthalmoscope light through the pupillary aperture onto the retina. Generally start with '0' lens of the ophthalmoscope and adjust the appropriate lens so as to get a clear vision of the disk margins.

Identify the following structures—arteries, veins, optic disk, macula, fovea and remaining parts of the retina. To get a proper view of the various media of the eye such as cornea, lens, and vitreous, start examination with +10 lens. Then the cornea will be in focus. Reduce the strength of the lens in order to bring the other structures into focus.

Normally, retinal arteries are vessels of smaller caliber which look orange-red with a pale strip in the center along their length. They are nonpulsatile. They are crossed by retinal veins which are larger, dusky red in color, more sinuous, less angular, and pulsatile. Normal venous pulsations can be brought out better by applying light pressure on the eye with the fingers or by asking the patient to do Valsalva maneuver.

The optic disk is located at the nasal side of the center of the posterior pole of the eye. It is pink in color, but paler than the surrounding retina, circular or slightly oval in shape, with a distinct margin all around. Compared to the temporal margin the nasal side is less sharp. Optic cup is that portion of the optic disk which is deeper than the rest of the disk occupying less than 1/3 of the disk area and usually eccentric in position. The arteries and veins of the retina pass through the optic cup. Lamina cribrosa consists of pearly white fibers arranged in a sieve like fashion at the floor of the optic cup.

The macula is situated laterally on the temporal side of the optic disk. It is of the same size as the optic disk, darker in color and slightly depressed from the retinal surface. It can be easily brought to focus by asking the patient to look into the light of the ophthalmoscope. The fovea is at the center of the macula and it appears as a yellowish white reflecting point.

Nonpathological curiosities if present, should be noted. These should not be mistaken for disease. These are:

i. Drusen bodies which are glistening structures over the optic disk.
ii. Myelinated nerve fibers which are opaque nerve fibers appearing as bright feather-like patches radiating for a short distance from the margins of the optic disk.
iii. Smaller or hypoplastic optic disk.
iv. Large sized disk or megalopapilla.
v. Tilted and obliquely elongated optic disk.
vi. Coloboma which is a small pit-like depression in the temporal region of the optic disk.

Assessment of Optic Disk Elevation in Papilledema

Start the ophthalmoscopic examination with a +10 lens. Gradually reduce the strength of the lens until the retinal vessels are seen distinctly. Note the strength of the lens used. Repeat the procedure to focus the vessels on the optic disk and again note the strength of the lens. The difference between these two values indicates the swelling of the optic disk in diopters. An elevation of 1 mm is reflected as 3 diopters.

Pseudopapilledema

In some individuals, even in the absence of disease, the optic disk margins are not very distinct and the cup may appear to be obliterated. This may superficially resemble papilledema, but some features help to distinguish these two conditions. In pseudopapilledema, the elevated optic disk is smooth and glistening, the vessels on its surface are clear, retinal arteries and veins are of normal caliber and venous pulsations are visible. There will not be any retinal hemorrhages or exudates. The appearances do not change with passage of time.

Common abnormalities of the optic disk seen are papilledema, papillitis and optic atrophy (Tables 32.9 and 32.10).

OCULOMOTOR, TROCHLEAR AND ABDUCENT NERVES—III, IV, AND VI CRANIAL NERVES

Anatomy

The oculomotor, trochlear and abducent nerves are described together, since these three nerves and the muscles innervated by them participate in the smooth and coordinated movements of the eyes.

Table 32.9: Features that distinguish papilledema from papillitis

Optic disk	*Papilledema*	*Papillitis*
Color	Hyperemia due to telangiectasia of normal capillaries	Deep red
Cup	Obliterated or slightly elevated due to passive transudation of fluid (choked disk)	Obliterated and elevated markedly due to inflammation of the optic nerve head (papillitis)
Contour	The margins are indistinct, due to opacification of nerve fibers in peripapillary zone starting from the upper nasal quadrant, then proceeding to superior, inferior and lastly temporal margin. This is the most specific sign of papilledema	Indistinct
Capillaries	Dilated	Dilated
Lamina cribrosa	Indistinct	Indistinct
Retina veins	Earliest change is loss of pulsations, later they become dilated and more tortuous	Pulsations are present but the veins may be dilated
Arteries	Constricted	Normal
Hemorrhages	Multiple, flame-shaped or linear hemorrhages around the optic disk	May be present around optic disk
Visual acuity and visual fields	In general, loss of vision is much less marked. In uncomplicated cases there may be constriction of peripheral field, and enlargement of the blind spot. Visual acuity is either normal or there may be transient visual obscurations. In complicated cases the visual acuity is reduced abruptly due to hemorrhage or exudate in the macula	Visual acuity for central vision is suddenly reduced in one eye. Central field defects occur in the form of scotomas, but the peripheral field may remain normal in the early stage
Onset	Generally insidious	Acute
Symmetry	Usually bilateral	Usually unilateral
Pain Common causes	Generalized headache (a) Bilateral papilledema: Raised intracranial pressure due to any cause, malignant hypertension, toxemia of pregnancy. Less common causes are severe emphysema, severe anemia, hypoparathyroidism and Guillain-Barrè syndrome. (b) Unilateral papilledema: Orbital tumors, central retinal vein occlusion, papillophlebitis. *Note:* Under certain conditions papilledema may not develop even when the intracranial pressure rises. These include pre-existing optic atrophy, severe myopia and presence of adhesions in the subarachnoid space around the optic nerve.	Pain in and around the affected eye Toxic agents such as tobacco, methyl alcohol, lead, quinine, and others infections demyelination and multiple sclerosis. In some cases, it is idiopathic.

OCULOMOTOR NERVE—III CRANIAL NERVE

Applied Anatomy

This nerve has two major nuclei:

i. Main motor nucleus
ii. Accessory or parasympathetic nucleus (Edinger-Westphal nucleus).

The main motor nucleus is situated close to the midline in the gray matter that surrounds the cerebral aqueduct, at the level of the superior colliculi in the midbrain. It has several subnuclei that innervate different extraocular muscles. The ventral, dorsal and intermediate subnuclei supply the ipsilateral medial rectus, inferior rectus and inferior oblique muscles respectively, whereas the medial subnucleus supplies the superior rectus muscle in the opposite eye through the opposite III nerve. The caudal subnucleus supplies the levator palpebrae superioris muscles of both eyes. The parasympathetic subnucleus which lies dorsal and rostral to the main nucleus supplies the ciliary and constrictor pupillae muscle of the iris on both sides. The fibers innervating the medial rectus, inferior rectus and inferior oblique muscles are uncrossed. Those to the superior rectus are crossed and those to the levator palpebrae superioris, ciliary muscle and constrictor pupillae of the iris are completely mixed, i.e. both crossed and uncrossed. Hence, a nuclear lesion of the III cranial nerve on one side results in paralysis of the medial rectus, inferior rectus and inferior oblique muscles with bilateral ptosis and

Table 32.10: Differential diagnosis of primary and secondary optic atrophy

	Primary optic atrophy	*Secondary optic atrophy*
Optic Disk	Whole or a part affected	Entire disk affected
Color	Chalky white	Grayish white
Cup	Increased in size and depth	Obliterated
Contour	Distinct	Indistinct
Capillaries	Reduced in number (Kestenbaum's sign) Normal number is about 10	Normal
Lamina cribrosa	Prominent	Indistinct
Retina		
Veins	Normal	May be dilated
Arteries	Normal	May be constricted
Hemorrhages and exudates	Absent	May be present
Vision	Usually affected in the vast majority of cases. Rarely, if the disease process recovers or it does not affect the papillomacular bundle, vision may be retained.	Usually affected
Symmetry	Unilateral or bilateral	Usually bilateral, but may be unilateral
Common causes	(a) *Acquired:* Optic neuritis, compression injury, or ischemia of optic nerve, retinal artery occlusion, diabetes mellitus, atherosclerosis, anemia, deficiency of thiamine and cyanocobalamin, toxic amblyopia due to tobacco, lead, methyl and sometimes ethyl alcohol, drugs like ethambutol, INH, chloroquine, quinine, and others, neurosyphilis, neurotuberculosis. (b) *Inherited:* Leber's optic atrophy, other types of hereditary optic atrophies.	Secondary to papilledema of long duration

superior rectus involvement on the opposite side. Bilateral nuclear lesion may at times spare the central subnucleus innervating levator palpabrae superioris and hence ptosis may be absent. Thus a nuclear III cranial nerve affection is often incomplete. For the same reason, a unilateral total III nerve palsy with normal contralateral superior rectus is unlikely to be due to lesion at nuclear level.

The oculomotor nerve after its formation from the nuclei emerges on the anterior surface of the midbrain in the interpeduncular fossa. It passes anteriorly between the superior cerebellar and posterior cerebral arteries and travels forward in close relation to the posterior communicating artery before entering the lateral wall of the cavernous sinus, where it divides into superior and inferior branches. These branches pass forward to enter the orbit through the superior orbital fissure. Because of this course of the nerve, it is more vulnerable for compression in temporal lobe herniation associated with supratentorial space occupying lesions and in aneurysms of the neighboring arteries.

In temporal lobe herniation, this nerve often gets compressed at the tentorium cerebelli. The superior branch of the nerve supplies the superior rectus and levator palpebrae superioris, whereas the inferior branch supplies the medial rectus, inferior rectus and inferior oblique muscles, constrictor pupillae and the ciliary muscle. The fibers of the III nerve form the efferent pathway for the pupillary light reflex and accommodation reflex.

The nerve fibers to the constrictor pupillae of the iris are thin and situated at the periphery of the main trunk of the III nerve on its superomedial aspect. These fibers receive their blood supply mainly from the perineural vascular plexus in contrast to the other fibers in the nerve which are supplied by the penetrating vasa nervosum. Because of these anatomical features, compressive lesions of III nerve lead to ipsilateral pupillary dilatation and loss of light relfex as the earliest sign, whereas ischemic lesions of the nerve usually spare the pupil. The other signs of III nerve paralysis like ptosis and extraocular muscle palsies appear much later, in the course of temporal lobe herniation.

TROCHLEAR NERVE—IV CRANIAL NERVE

The nucleus of this nerve is situated in the gray matter that surrounds the aqueduct in the midbrain at the level of the inferior colliculi. After leaving the nucleus the nerve fibers pass posteriorly around the central gray matter in the substance of the midbrain and on reaching its dorsal surface, decussate in the superior

medullary velum with the fibers from the nucleus of the opposite side. The nerve then passes anteriorly, enters the lateral wall of the cavernous sinus and then passes forward to enter the orbit through the superior orbital fissure. It supplies the superior oblique muscle. The two unique features of this nerve are: (i) it is the only cranial nerve which decussates between its nucleus and its point of exit from the brainstem and (ii) it is also the only cranial nerve that emerges on the dorsal aspect of the brainstem. Because of this anatomical arrangement, a nuclear lesion of IV nerve results in paralysis of superior oblique muscle on the opposite side whereas infranuclear lesion leads to paralysis of this muscle on the same side. However, isolated involvement of IV nerve or its nucleus is rare.

ABDUCENT NERVE (SYN: ABDUCENS NERVE)—VI CRANIAL NERVE

The nucleus of this nerve is situated beneath the floor of the fourth ventricle near to the midline in the pons. Fibers from this nucleus pass anteriorly and the nerve emerges at the junction between the pons and the medulla oblongata. It then passes through the cavernous sinus and enters the orbit through the superior orbital fissure. It supplies the lateral rectus muscle. This nerve may have several anatomical variations in its origin and course. It may arise as two distinct trunks or it may split into two branches. If only one of such branches is affected in a disease process, the result may be only partial weakness of the lateral rectus muscle instead of its total paralysis. Lateral rectus paresis or paralysis often develps as false localizing sign in raised intracranial pressure. Irrespective of the side and site of the causative lesion leading to intracranial pressure, the VI cranial nerve is subjected to greater pressure as it passes over the sharp upper surface of the petrous temporal bone and this leads to its paralysis.

The fiber connections of III, IV and VI cranial nerve nuclei include the following:

i. Corticonuclear fibers from both cerebral hemispheres.
ii. Tectobulbar fibers which connect these nuclei to the visual cortex through the superior colliculus.
iii. Fibers from the medial longitudinal fasciculus (MLF) by which these nuclei are interconnected with each other, and to the vestibular nuclei and also to other structures in the brainstern.

Tests of Function of Oculomotor Nerves

1. Test for levator palpebrae superioris.
2. Tests for ocular movements (Figs 32.4 to 32.7).
3. Tests for pupils.
4. Tests for squint.
5. Tests for diplopia.
6. Tests for nystagmus.

Test for Levator Palpebrae Superioris

The levator palpebrae superioris is a voluntary muscle that helps to elevate upper eyelid. Normally, the upper eyelid covers about 0.5 to 1.0 mm of the upper portion of the cornea, when the eye is in neutral position. In this position, the lower eyelid margin just touches the lower border of the cornea. Paralysis of levator palpebrae results in ptosis, i.e. drooping of the upper lid with consequent narrowing of the palpebral fissure. Ptosis may be total or partial. Partial ptosis has to be differentiated from a narrow palpebral fissure that results from enophthalmos or blepharospasm in which the palpebral fissure is narrowed from above and below.

Muller's muscles in the upper and lower eyelids are involuntary muscles supplied by the sympathetic nerves and these muscles are in a state of tonic contraction. Sympathetic paralysis leads to loss of tone of Muller's muscles resulting in partial ptosis of the upper lid and elevation of the lower lid. Ptosis due to sympathetic palsy is always partial and the upper lid can be raised voluntarily to some extent. Ptosis due to III nerve may be total or partial and voluntary elevation of the eyelid is not possible in complete paralysis. The frontalis muscles may compensate to overcome the drooping and this may lead to prominent wrinkling of the forehead.

Test: Ask the patient to look at a distant object, keeping the eyes in primary position. Observe the width of the palpebral fissure on both sides and compare. Note the extent of cornea covered by the upper and lower eyelids. Ask him to voluntarily elevate the upper lids. Also observe the degree of frontalis muscle contraction on both sides.

Neurological causes of ptosis include III nerve palsy, sympathetic palsy, myasthenia gravis and

ocular myopathies (Fig. 32.8). Ptosis due to these lesions can be distinguished clinically.

III Nerve Palsy

Ptosis is usually total but can be partial and voluntary elevation of the eyelid is defective. Frontalis muscle may be in a state of contraction in an attempt to elevate the eyelid (Figs 32.4 and 32.5).

Pupil is dilated, other extraocular muscles supplied by III nerve may also be affected (Fig. 32.5)

Sympathetic Palsy

Ptosis is partial and voluntary elevation of the upper lid is possible. Pupil is constricted (miosis).

Other components of sympathetic palsy such as enophthalmos (retraction of eyeball) and anhydrosis (absence of sweating) on the same side of face may be present. These features constitute Horner's syndrome.

Myasthenia Gravis

Ptosis may be partial or total, usually bilateral, symmetrical, depending on the severity of the disease and fatigue of the muscles. The ptosis shows diurnal variation, often being worse towards the evening. Pupils are normal. Other extraocular muscles and limb muscles may also be affected. The weak muscles respond promptly to an injection of prostigmine.

Ocular Myopathy

Ptosis is usually bilateral and progressive, without showing diurnal variation. Pupils are normal.

Other extraocular, pharyngeal and limb muscles may also be affected. There is no significant response to neostigmine.

Partial ptosis can also occur in local ocular conditions such as trachoma and tumors of the eyelid. Rarely, it can be congenital in which case it is usually bilateral. The Gunn phenomenon is the exaggerated elevation of the eyelids on opening the mouth or during jaw movements. This is seen in some cases of congenital ptosis due to pathologic synkinesis. Involuntary eye closure on jaw opening is called inverse Gunn phenomenon.

Tests for Ocular Movements

The eyes can be moved voluntarily in horizontal, vertical and diagonal directions. Horizontal movements outwards and inwards are called abduction and adduction. Vertical movements upwards and downwards are called elevation and depression. Rotation of the eye towards the nose is called internal rotation or intorsion and away from the nose is called external rotation or *extorsion.* These rotatory movements are not possible voluntarily. In health they occur as normal associated movements during acts such as reading. In paralysis of individual ocular muscles rotation occurs due to unopposed action of other muscles.

Abduction of the eye is brought about by the lateral rectus and adduction by the medial rectus (Figs 32.6 and 32.7). Elevation of the eye in the abducted position is brought about by the superior rectus and in the adducted position by the inferior



Fig. 32.4: Third nerve palsy left showing complete ptosis due to paralysis of levator palpebrae muscle. Note also wrinkling of the forehead in an attempt to elevate the eyelid



Fig. 32.5: Third nerve palsy–Note the absence of medial movement of the left eye due to paralysis of medial rectus



Fig. 32.6: Paralysis right lateral rectus



Fig. 32.7: Paralysis left lateral rectus



Fig. 32.8: Case of bilateral ptosis and partial ophthalmoplegia in an elderly patient—a case of ocular myopathy

oblique. Depression of the eye in the abducted position is brought about by the inferior rectus and in the adducted position by the superior oblique. In mid position of the gaze, the elevation of the eyes is brought about by two muscles, namely superior rectus and inferior oblique, and depression also by two muscles, namely inferior rectus and superior oblique. It should be noted that the superior and inferior recti muscles act as sole elevators and depressors when the eye is in abducted position, and the oblique muscles act similarly when the eye is in adducted position. Medial and lateral recti act in the horizontal plane. Vertical as well as horizontal movements of the eyes made from the mid-position of gaze are called "cardinal" movements. The normal range of eye movement in complete adduction is about 50° medially so that the inner margin of the cornea gets buried under the caruncle and in complete abduction about 60° laterally so that the outer margin of the cornea reaches the outer canthus. In the vertical plane, they move 30° upwards and 50° downwards.

Normally, the movements of both eyes are symmetrical, so that their visual axis converge at the point at which the gaze is fixed. These movements are called "conjugate" movements. They are controlled by the centers situated mainly in the frontal and occipital cortex and in the brainstem, through supranuclear and internuclear connections of III, IV and VI cranial nerve nuclei. For proper eye movements, the lower motor neurons of III, IV, and VI cranial nerves and their connections to the extraocular muscles should be intact. In addition, their supranuclear and internuclear connections should also be normal (Table 32.12).

Whereas nuclear and infranuclear lesions of III, IV, and VI cranial nerves lead to paralysis of individual extraocular muscles, supranuclear lesions lead to paralysis of conjugate movements of the eyes. Examination of ocular movements is of great importance in neurological diagnosis.

Examination of individual extraocular muscles: Function of individual extraocular muscles should be tested in each eye separately, although both eyes move together even when testing them individually. The patient, sitting up or lying down is asked to follow with his eyes the movement of the examiner's finger, held about 60 cm away from the patient's face and moved in the following 8 directions—to the right, and left in the horizontal, upwards and downwards when the eye is in abducted and adducted positions and upwards and downwards in the neutral position. The patient is not allowed to move his head. If necessary, the examiner may hold the patient's head with his left hand to prevent it from moving. The range of movements of the eye in each direction is observed. Presence of diplopia should also be enquired into.

In paralysis of extraocular muscles the movements mediated by them are absent or weak and diplopia commonly occurs when the paralyzed muscle is put into action.

The muscle pairs which move the eyes conjugately in different directions are shown in the (Flow chart 32.2).

Note: The names of the muscles in a given pair that move the eyes in the vertical plane are exactly opposite to each other. For example, the two muscles which move the eyes upwards and to the right are right superior rectus and left inferior oblique muscles. Also refer to Figure 48.2, Chapter 48 (Normal movements of the eyeball)

Nuclear and infranuclear ophthalmoplegia (LMN lesion) nuclear and infranuclear lesions of III, IV and VI cranial nerves lead to:

i. Paralysis of individual eye muscles or group of muscles
ii. Squint
iii. Abnormal head position
iv. Diplopia.

The characteristic features of these three cranial nerve palsies are shown in Table 32.11. Total paralysis of III, IV and VI cranial nerves together is known as total ophthalmoplegia. Paralysis of only the extraocular muscles is called external ophthalmoplegia. Paralysis of the intrinsic muscles of the eye (ciliary and constrictor pupillae) is called

Table 32.11: Clinical features of isolated extraocular muscle palsies

	Signs of paralysis			
Extraocular muscle and its action	*Eye deviation (squint)*	*Head tilt*	*Movement affected*	*Diplopia*
Superior rectus—elevation of eye in abducted position	Downwards and outwards	Backwards and to affected side	Upward movement in abducted position	Crossed on looking up and outwards
Medial rectus—adduction of eye	Laterally (divergent squint)	Face turned to normal side	Adduction	Crossed on looking medially
Inferior rectus—depression of eye in abducted position	Upwards and outwards	Forward and to affected side	Downward movement in abducted position	Crossed on looking down and outwards
Lateral rectus—abduction of eye	Medially (convergent squint)	Face turned to affected side	Abduction	Uncrossed on looking to ipsilateral side
Inferior oblique—elevation of eye in adducted position	Downwards and inwards	Backwards and towards the shoulder on affected side	Upward movement in adducted position	Oblique, on looking upwards and inwards.
Superior oblique—depression of eye in adducted position	Rare, looking down from primary position produces extorsion of the eye	Foward and to normal side	Downward movement in adducted position	Uncrossed, oblique on looking downward and inwards

Flow chart 32.2: Muscles acting to move the eyeballs

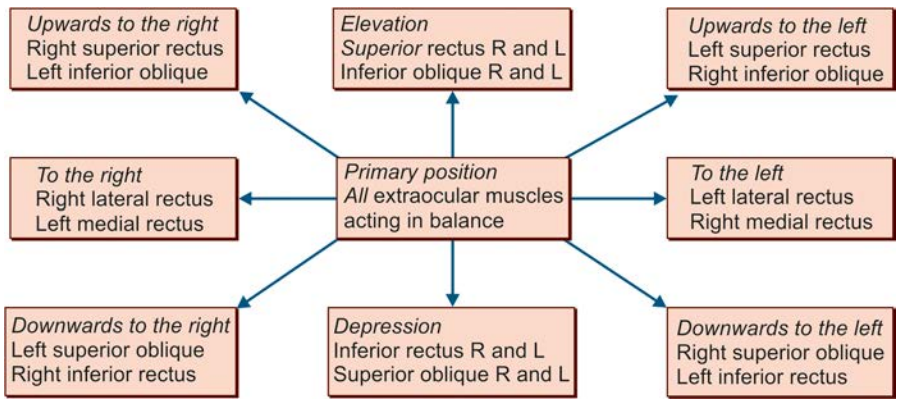


Table 32.12: Diagnostic features and causes in nuclear and infranuclear ophthalmoplegias

Site of lesion	*Neurological signs*	*Common causes*
1. *Lesion at the level of the nuclei*		
a. III Cranial nerve	i. Paralysis of ipsilateral medial and inferior recti, contralateral superior rectus and bilateral levator palpebrae	*Brainstem lesions:* Vascular disease, multiple sclerosis, poliomyelitis, Wernicke's encephalopathy, tumors, congenital agenesis of nuclei
	ii. Bilateral total III nerve palsy with or without ptosis	
	iii. Bilateral total III nerve palsy with or without pupillary involvement	do
b. IV Cranial nerve	Contralateral paralysis of superior oblique muscle	do
c. VI Cranial nerve	Ipsilateral paralysis of lateral rectus muscle	do
Note: Nuclear lesions are almost always associated with neighborhood signs such as other cranial nerve palsies and deficits due to involvement of ascending sensory and descending motor tracts, e.g. Weber's syndrome. Exception congenital agenesis of the nuclei.		
2. *Lesions distal to the nuclei*		
a. At the base of the brain	III, IV and VI cranial nerve palsies in different combinations with or without other cranial nerve palsies and signs of meningitis. Isolated III nerve palsy	Meningitis, nasopharyngeal carcinoma, cranial neuritis, basilar artery aneurysm. Aneurysm of posterior communicating artery, temporal lobe herniation due to raised intracranial pressure, vasculitis, neuritis, diabetes mellitus.
	Isolated IV nerve palsy (unilateral/bilateral)	Head trauma, diabetes mellitus, tumors of superior medullary velum.
	Isolated VI nerve palsy	Raised intracranial pressure of any etiology, vasculitis, neuritis, diabetes mellitus.
b. At petrous temporal bone	VI nerve palsy with VII, VIII and occasionally V nerve palsy. Isolated, transient (few weeks) VI nerve palsy in children	Petrositis (Gradenigo's syndrome) Following infection of middle ear or upper respiratory tract
c. At cavernous sinus (CS) Anterior portion of CS	III, IV, ophthalmic division of V and VI nerve palsies with or without optic nerve involvement. Associated signs are proptosis, chemosis and papilledema.	Cavernous sinus thrombosis—septic or aseptic
Middle portion of CS	III, IV and VI nerve palsies without optic nerve involvement	Aneurysm of intracavernous part of carotid artery.
Posterior portion of CS	Paralysis of III, IV, V (ophthalmic and maxillary divisions) and VI nerves	Carotico—cavernous fistula, pituitary tumors, craniopharyngioma, meningioma of cavernous sinus.
d. At superior orbital fissure and apex of the orbit	Paralysis of III, IV, ophthalmic division of V and VI nerves with or without optic nerve involvement. Associated signs—proptosis, reduced vision at times	Tumors such as meningioma, haemangioma, optic nerve glioma, neurofibroma, metastatic deposits and pseudotumour of the orbit, Tolosa Hunt syndrome, arteriovenous malformations in the orbit.
e. At neuromuscular junction	Unilateral or bilateral weakness of any or all of the extraocular muscles with ptosis. Pupils are spared. Diurnal variation of weakness is characteristic	Myasthenia gravis
f. Extraocular muscles	Weakness of any or all of the extraocular muscles with or without exophthalmos, occurring bilaterally pupils are spared. Other skeletal muscles may also be affected.	Myopathies, oculopharyngeal muscular dystrophies.

internal ophthalmoplegia. In total ophthalmoplegia, the pupil remains dialated and fixed. In myasthenia gravis and ocular myopathies only external ophthalmoplegia occurs.

Test for Pupils

Observe the pupils to assess their size, shape, and symmetry. Elicit the light reflex and accommodation reflex. The pupils should be examined under average, dim, and brightly illuminated conditions. (*See* also page 407 for the pathways)

Size and shape: Average diameter is 2 to 5 mm but it varies with the ambient illumination, age, mental activity and presence or absence of refractive error. Persons at extremes of age have small pupils whereas anxious persons and those with myopia have large pupils. Normal pupils are generally circular and central, but may be eccentric.

Both pupils are equal in size, but a difference in size up to 1 mm may be normal in 15 to 20% of subjects. If this difference persists irrespective of the ambient illumination, it can be considered as a normal variation, but if it changes, then it is pathological. Difference in the size of pupils is called anisocoria.

Rhythmic constriction and dilatation of pupil is called hippus. This may be a manifestation of disease, but rarely it may be a normal phenomenon without any neurological significance.

Light Reflex (Reaction to Light)

When light is thrown into one eye the pupil constricts. Using a sharply focussed pen torch direct the light from the sides at first into one eye and then into the other, taking care to see that the light does not fall into both eyes Simultaneously. Observe both pupils. Afferent for this reflex is the optic nerve and the efferent is the oculomotor nerve.

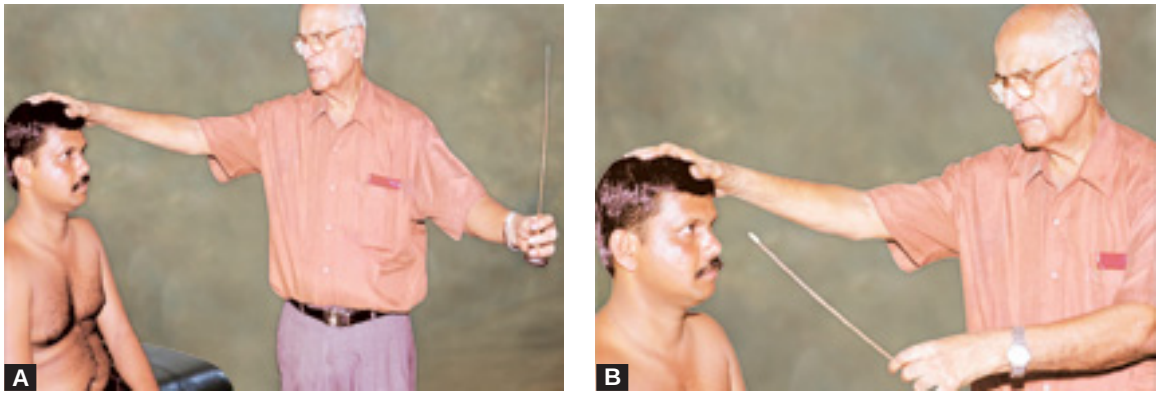
Constriction of the ipsilateral pupil in response to light is direct light reflex. Consensual response or indirect light reflex is the constriction of the opposite pupil when light is thrown into one eye (Fig. 32.9).



Fig. 32.9: Eliciting light reflex in the left eye. Description (see text)

Abnormalities of Light Reflex

1. The pupil may not respond in direct and consensual light reflex. This occurs in third nerve palsy. In most cases the pupil is dilated and fixed.
2. The pupil does not constrict in direct light reflex, but does so in consensual reaction. Often this is due to lesion in the afferent pathway, i.e. optic nerve lesion on the side of abolition of direct light reflex.
3. *Argyll Robertson pupil:* The pupils are small, constricted, and do not react to light reflex, but react to accommodation. The lesion is in the pretectal area. Argyll Robertson pupil is characteristically seen in tabes dorsalis and general paralysis of the insane. Associated features are absence of dilatation in response to mydriatrics like atropine. Inmost cases, the condition is bilateral. Vision is unaffected.
4. *Holmes-Adie pupil:* This is also known as 'tonic pupillary reaction'. The reaction to light appears to be absent, or it may be present but delayed and sustained. Accommodation reflex is also delayed and sustained, i.e. pupillary constriction proceeds even after convergence ceases. Tonic pupillary reaction is a benign condition in which the lesion is in the ciliary ganglion. Other accompaniments of 'tonic pupillary reaction' are absence of muscle stretch reflexes, especially the ankle jerk (Holmes Adie syndrome).
5. *Wernicke's hemianopic pupillary reaction:* In conditions where the visual afferent pathway is interrupted after the fibers for light reflex have left the optic tract, vision may be lost, but the reflex fibers being intact, the light reflex can be elicited by throwing light into the hemianopic visual field.



Figs 32.10A and B: Testing for accommodation reflex. (A) Patient looking at distant object, (B) Patient looking at near object. (*See* text for description)

Accommodation reflex *(Syn. reaction to accommodation):* This reflex occurs when the person focuses his vision on a near object.

Method of testing: The patient is asked to fix his eyes on the examiner's index finger which is held a meter away and then rapidly brought near to the patient's nose. Convergence of the eyes and pupillary constriction can be observed (Figs 32.10 A and B).

Ciliospinal reflex: When the skin over the neck is pinched, pupil on the same side dilates reflexly. This results from stimulation of the sympathetic fibers which supply dilator pupillae muscle.

Ciliospinal reflex is abolished in lesions of cervical sympathetic nerves, affection of the upper thoracic and cervical segments of the spinal cord, the medulla oblongata, and D_1 root.

Note: The following points should be kept in mind before assessing the significance of pupillary abnormalities.

1. Ensure that no drugs are applied to the patient's eye, e.g. miotics such as pilocarpine and mydriatics such as homatropine.
2. If the pupils are unequal in size decide which side is the abnormal one. In the presence of ptosis or weakness of the extraocular muscles, the pupil in that eye is most likely to be the abnormal one.

Squint

Squint or strabismus is defined as abnormal position or deviation of the eyes, resulting in loss of parallelism in the visual axis of both eyes. The abnormal deviation of the eye may be divergent, convergent, upwards or downwards. It may affect one eye or both eyes alternately. If it is noticeable when both eyes are kept open it is called manifest squint. If it can be detected only by covering one eye it is called latent squint. Basically, there are two types of squint—paralytic and non paralytic or concomitant. Paralytic squint results from paralysis of a muscle or a group of muscles acting on the eyeball. Squint manifesting without paralysis of extraocular muscles is called nonparalytic squint (concomitant squint). The vision in the squinting eye, in the case of nonparalytic squint, is defective from early childhood. In paralytic squint, the abnormality may be obvious when the eyes are in the resting position and it becomes accentuated when the eyes are turned in the direction of action of the paralysed muscle. The images of an object fail to fall on corresponding points in the retina of both eyes and this leads to diplopia. On the other hand, in nonparalytic squint, the squint may be obvious at rest, but it remains the same in all positions of the eyes. The movements of the affected eye are normal on testing and there will be no diplopia.

In paralysis of medial rectus and superior oblique muscles, the squint is divergent due to unopposed action of the lateral rectus, and in paralysis of the lateral rectus, it is convergent due to unopposed action of the medial rectus. Upward or downward paralytic squint is rare. Sometimes, divergent squint may occur in high degree of myopia and in deep coma.

Test for Squint

1. Examine the eyes in the resting position and note the loss of parallelism of the eyeballs (Figs 32.11 and 32.12). The squint can be made more prominent by moving the eyeball towards the side of action of the abnormal muscle. In paralytic squint the diplopia develops. The images from both eyes gets separated, the image from the normal eyes is bright (true image) whereas one from the paralyzed eye is less so (false image). In non-paralytic squint the eyeball moves in all directions and there is no diplopia.

Cover Test

This is done to assess the primary and secondary deviation of the eyes, when the patient has squint.

Instruct the patient to fix his gaze on an object immediately in front of him. Suddenly cover the apparently fixing eye, with your hand so that the other eye fixes on the object. If the uncovered eye makes any movement to take up fixation, it is called primary deviation. If the covered eye also deviates, it is called secondary deviation. Note the degree of primary and secondary deviations of the eyes.

In nonparalytic squint, the primary and secondary deviations of both eyes will be equal in all positions of the eyes. In paralytic squint, the secondary deviation of the normal eye will be greater than the primary deviation of the affected eye and the angular deviation of the two visual axes varies with different position of the two eyes.



Fig. 32.11: Left divergent squint



Fig. 32.12: Child with esotropia-right convergent squint

Diplopia

Diplopia or double vision is said to be present when patient complains of seeing two images when he looks at one object. This symptom is usually associated with paralysis of one or a group of extraocular muscles, which may or may not be obvious clinically. Due to paralysis of extraocular muscles, the movements of the affected eye will be defective and this results in loss of parallelism of the visual axes of both eyes. As a consequence of this, the image of an object falls directly on the macula of the normal eye but at some distance away from the macula in the affected eye. Binocular fusion of these two images arising from different, noncorresponding points on the two retinae cannot occur in the visual cortex and therefore the patient perceives two separate or overlapping images. The image from the macula of the normal eye will be clear and it is called true image. The image from the affected eye will be indistinct and it is called false image. Many patients can recognize which of the two images is true and which is false. Sometimes, they can also tell in which direction of gaze the diplopia occurs or maximal separation of the two images takes place.

Test

First determine whether diplopia is binocular, i.e. diplopia occurring when looking with both eyes or monocular, i.e. diplopia occurring when looking with only one eye. Monocular diplopia is almost always due to local ocular causes such as astigmatism, cataract and retinal detachment. It can also occur in hysteria. Once it is established that diplopia is binocular, the patient is asked to look in all the nine directions of gaze to detemine in which position maximal separation of the true and false images occurs.

From that position of the eyes, the paretic muscle can be ascertained because maximal

separation of the two images occurs when the eyes are moved in the direction of action of the weak extraocular muscle. The abnormal eye can be determined by covering one eye and noting the effect on the diplopia. If this results in disappearance of the false image, then the paretic muscle belongs to that eye. When it is difficult to determine the abnormal eye in cases where diplopia occurs in the absence of visible squint, a red glass test can be performed to resolve the issue.

Red Glass Test

With the patient in sitting position, keep a red glass in front of his right eye and a colorless or plain glass in front of the left eye. Keeping his head fixed, ask him to look at an object such as a lighted candle, kept at a distance of about 0.5 m in front. Move the object slowly in all the cardinal directions of gaze and instruct the patient to indicate any blurring or double vision which may occur and also in which position, the separation of the two images is greatest. Applying the following rules, the paretic extraocular muscle can be identified.

i. The distance between the true and false images will increase when the patient looks in the direction of action of the paretic muscle.
ii. The outer image is always the false image, seen by the abnormal eye. This eye can be identified by the color of the outer image. Both diplopia and squint tend to come down in severity and may even disappear as time passes.

NYSTAGMUS

Nystagmus is defined as involuntary, usually rhythmic oscillations of the eyes without an appreciable interval between consecutive oscillations. Most often, it is a manifestation of disturbed ocular movement due to a neurological disease. Sometimes, it may also result from disorders of the eyes and vestibular apparatus. The basic defect in nystagmus is failure to maintain the eyes in a certain position.

Whenever there is nystagmus, the following aspects should be observed:

i. Type.
ii. Direction.
iii. Rate.
iv. Amplitude.
v. Intensity
vi. Duration of the oscillatory movements of the eyes. Based on this information, a clinical classification of nystagmus may be made which gives a clue to the possible site of the causative lesion.

Types of Nystagmus

Depending on the beat mode of the oscillations of the eyes, broadly two types of nystagmus are recognized. These are:

a. Pendular nystagmus, in which the eyes move to and fro towards either side of a central point, resembling the swing of a pendulum.
b. Jerk nystagmus, in which the movement of the eyes is faster in one direction and slower in the other direction. In other words, this nystagmus has two phases-slow and fast (jerk), By convention, the direction of jerk nystagmus is designated by its fast phase because it is more easily recognizable than the slow phase. "nystagmus to left" means the fast phase is to the left and "nystagmus to right" means the fast phase is to the right of the patient.

Direction of Nystagmus

The direction of the oscillatory movements of the eyes may be horizontal, vertical or rotary.

Rate

The rate of the oscillations is variable. It may be slow (10-40 oscillations/mt), medium (40-100/ mt), or rapid (more than 100/mt).

Amplitude

If the amplitude of the oscillations of the fast phase is less than 1 mm, it is described as fine nystagmus, if it is 1 to 3 mm, as medium nystagmus and if it is more than 3 mm, as coarse nystagmus.

Intensity

This applies only to jerk nystagmus. This can be graded into 3 degrees:

First degree or grade 1: Nystagmus will be present only when the patient looks towards the direction of the fast phase of the nystagmus.

Second degree or grade 2: Nystagmus will be present not only while looking in the direction of its fast phase, but also in the primary position of the eyes.

Third degree or grade 3: Nystagmus will be present even when the patient looks in the direction opposite to that of its fast phase.

Duration

Nystagmus may be unsustained, being noticeable only for a very brief period or it may be sustained for longer periods.

Test

Always look for nystagmus under good illumination. First observe the eyes in their primary position. In this position, congenital pendular nystagmus and second degree jerk nystagmus can be detected. Then ask the patient to look for a few seconds at least, at your finger held at about 60 cm in front of his eyes, to the right and to the left of the midline, so that the eyes deviate not more than 30° from the primary position. Horizontal nystagmus is detected in these two positions. Vertical nystagmus can be detected by asking the patient to look at your finger held at a level just above or below the level of the primary position of the eyes. A special type of vertical nystagmus called down-beat nystagmus (see below) is brought out prominently in the lateral gaze position of the eyes.

Note: While testing for nystagmus, the finger should not be held too close to the patient's eyes so as to avoid the accommodation reflex. Similarly, extremes of gaze should be avoided because even normal individuals may show nystagmus in these positions due to muscle fatigue, especially if the gaze is maintained for more than 30 seconds. Anxious individuals may show nystagmus within 1 to 2 mm of extreme abduction and adduction of the eyes. In both these situations, the oscillatory movements of the eyes will be irregular and ill sustained and they are not pathological. They are more correctly termed as 'nystagmoid' movements.

Clinical Significance of Nystagmus

Presence of nystagmus suggests disturbed mechanisms of ocular posture or position. Normally impulses from the retina, extraocular muscles, vestibular nuclei and neck muscles reach the brain to convey information about the position of the eyes relative to the head, body and environment. These afferent impulses help to maintain tone and muscle contraction of the agonist and antagonist extraocular muscles, thereby keeping the eyes steady in different postures. If this balancing mechanism is disturbed, the eyes tend to drift in one or other direction which gives rise to the slow phase. As a corrective phenomenon the eyes are brought back to the neutral position as the quick phase, only to drift back again. These cycles of drift and corrective movements in opposite directions give rise to nystagmus.

In many cases, the nystagmus is conjugate with co-ordinated movement of both eyes. Occasionally it is dysconjugate with the eyes converging and diverging or moving up and down in opposite directions. Rarely, unilateral nystagmus occurs in conditions like amblyopic squint, astigmatism, high refractive error or internuclear ophthalmoplegia.

The cause of nystagmus may be a defect in visual fixation, gaze mechanism, vestibular mechanism, or the convergence mechanism.

Nystagmus Due to Defective Visual Fixation

This type of nystagmus occurs only in forward gaze. It is due to a defect either in the afferent or efferent pathway for ocular fixation. Defects in the afferent pathway result in 'ocular fixation nystagmus' and defects in the efferent pathway result in 'neurological fixation nystagmus'.

Ocular Fixation Nystagmus

It occurs due to defective vision, because of which the patient makes searching movements of the eyes in a vain effort to find a fixation point. In most cases the defective vision occurs early in infancy before normal macular fixation fully develops. Several congenital conditions such as bilateral macular defects, cataracts, aniridia, high degree of astigmatism, myopia, total color blindness and albinism are common causes for fixation nystagmus. Acquired causes such as bilateral corneal opacities due to ophthalmia neonatorum and macular choroiditis due to toxoplasmosis also can lead to the same. The nystagmus seen in these conditions is usually a horizontal pendular nystagmus, present in forward gaze. Its amplitude increases on lateral gaze, and decreases on attempting to fixate on a near object. It ceases when the eyes are closed. Once established, it persists throughout life.

Different Types of Ocular Fixation Nystagmus

a. *Hereditary nystagmus:* This is a pendular nystagmus in forward gaze and horizontal jerk nystagmus on lateral gaze, manifesting within a few weeks of birth and persisting throughout life. It shows X-linked transmission.
b. *Latent nystagmus:* This is a jerk nystagmus of both eyes which becomes evident only when one eye is occluded. The fast phase is towards the nonoccluded eye. It is also probably a variety of hereditary nystagmus. Usually, it is associated with strabismus and markedly reduced visual acuity on occluding one eye.
c. *Occupational or miner's nystagmus:* This is a rapid, rotary nystagmus that increases on upward gaze and decreases on downward gaze, seen in persons who have worked for many years under poor illumination such as in mines.

'Neurological' Fixation Nystagmus

This nystagmus is mainly due to lesions in the brainstem, the vision being normal.

a. A pendular nystagmus on forward gaze which changes into horizontal jerk nystagmus on lateral gaze and vertical nystagmus on upward gaze, occurs rarely in brainstem demyelinating disease and vertebrobasilar insufficiency.
b. See-saw nystagmus is another rare type of nystagmus characterized by pendular-rotatory nystagmus in which one eye moves up and rotates outwards and the other eye moves down and rotates inwards rhythmically. It is usually seen in lesions of middle cranial fossa such as pituitary tumors compressing the optic chiasma and distorting the brainstem. The exact mechanism of this nystagmus is not known.
c. Periodic, alternating nystagmus is also rare and it is characterized by horizontal jerk nystagmus which changes its direction spontaneously at set intervals of about 90 seconds. It is seen in lesions of lower brainstem.

Nystagmus due to Defective Gaze Mechanism

Pathological gaze related nystagmus occurs under the following conditions:

a. When there is internuclear or infranuclear ocular palsy, i.e. 'gaze type nystagmus'.
b. When there is supranuclear ocular palsy, i.e. gaze paretic or true gaze nystagmus.
c. When the gaze is directed up or down or laterally in the absence of ocular palsies, i.e. gaze-evoked nystagmus.
 - Gaze-type nystagmus. This occurs:
 1. When there is extraocular muscle paresis either due to a lesion in III, IV or VI cranial nerve or due to myasthenia gravis.
 2. When there is internuclear ophthalmoplegia due to a lesion in the medial longitudinal fasciculus (MLF).

Nystagmus due to extraocular muscle paresis is a jerk nystagmus that appears only when the eyes are moved in the direction of action of the weak extraocular muscle. The fast phase of the nystagmus is always towards the side of gaze that evokes the nystagmus. Although the nystagmus is seen in both eyes, it is greater in the eye with paretic muscle.

Nystagmus due to a lesion in medial longitudinal fasciculus (MLF) is a jerk nystagmus confined to the abducting eye brought on by attempting to look to one side, the other eye does not adduct correspondingly, or does so only minimally. In these conditions, there is no true gaze paresis.

Internuclear Ophthalmoplegia

This occurs when there is a lesion of the MLF usually in the pons or in the midbrain. On looking to the side opposite to the lesion, the ipsilateral eye stops short in adduction, whereas the opposite eye abducts, but shows nystagmus. The ipsilateral eye can adduct during convergence.

In lesions higher up in the brainstem, the medial rectus nucleus will also be involved along with MLF and this results in total loss of adduction of the ipsilateral eye both during lateral gaze to the opposite side and during convergence.

The term 'one-and-a half syndrome' refers to the condition where the lesion involves the MLF and the abducent nucleus on the same side. This leads to internuclear ophthalmoplegia with loss of abduction on the same side of lesion.

Gaze Paretic or True Gaze Nystagmus

This occurs when there is paresis of gaze due to a lesion either in the frontomesencephalic pathway

or in the paramedian pontine reticular formation (PPRF). Lesions in frontomesencephalic pathways produce either horizontal or vertical nystagmus depending on the type of gaze paresis whereas lesions in PPRF produce horizontal nystagmus. The resultant nystagmus is a jerk nystagmus that develops only on deviation of the eyes, with fast phase towards the side of the gaze. If the nystagmus appears on gaze to the right and to the left, at an equal distance from the primary position, it is called symmetrical gaze-paretic nystagmus. This is characteristic of multiple sclerosis and Friedreich's ataxia. It also occurs in drug toxicity, degenerative disease of brain and vascular and neoplastic diseases of the brainstem. On the other hand, if the horizontal nystagmus on gaze to the right and to the left are of different intensity and occur at different distances from the primary position, it is called asymmetrical gaze-paretic nystagmus and this is seen in unilateral lesions of PPRF. Unilateral lesion of fronto mesencephalic pathway results in gaze paresis and gaze-paretic nystagmus only for a short duration, whereas unilateral lesion of PPRF results in persistent gaze paresis and gaze-paretic nystagmus.

Lesions at the level of superior and inferior colliculi (e.g. Parinaud's syndrome), lead to isolated, up or down jerk nystagmus and paresis of upward or downward gaze.

Gaze-Evoked Nystagmus

In this condition, there is neither extraocular muscle palsy nor gaze palsy. Ocular movements are normal. Nystagmus occurs either in primary position or during lateral, upward or downward gaze. Hence, it is called gaze-evoked nystagmus. It usually occurs in lesions of brainstem and cerebellum, especially if flocculonodular lobe or fastigeal nuclei or their connections are affected. The resultant nystagmus is a jerk nystagmus, either horizontal or vertical. Up-beat nystagmus is a jerk nystagmus of large amplitude in the primary position, with fast phase upwards, that increases on upward gaze but decreases on downward gaze. It usually occurs in lesions of the anterior vermis of the cerebellum and rarely it can be congenital or drug induced. Down beat nystagmus is a jerk nystagmus with fast phase downwards, prominently seen on lateral gaze. It is characteristically seen in lesions at the level of cranio-vertebral junction such as Arnold Chiari malformation, basilar invagination, foramen magnum meningioma and others. It results from an impairment of spinovestibular input. Lesions limited to lateral lobes of the cerebellum do not produce nystagmus.

Nystagmus Due to Defective Vestibular Mechanism

This is called vestibular nystagmus. It may be peripheral when the lesion is in the labyrinth or vestibular division of VIII cranial nerve or 'central' when the lesion is in the vestibular nuclei or their connections. Vestibular nystagmus is always a jerk nystagmus, usually with a definite rotary component. It can be first, second or third degree in intensity.

Peripheral vestibular nystagmus is always horizontal and never vertical. It is always associated with vertigo. It usually results from destructive lesions of labyrinth or vestibular nerve and in such cases, the fast phase of nystagmus is towards the side opposite to the lesion. It does not change its direction with change of gaze. Irritative lesions of labyrinth are usually subclinical in their manifestations.

Central vestibular nystagmus is usually horizontal-rotatory, but can be vertical. It is horizontal when the middle portion of Dieter's or lateral vestibular nucleus is affected, vertical when its superior portion is affected and rotatory when its inferior portion is affected. The fast phase of nystagmus changes with the direction of gaze. It is always towards the side of the gaze and hence it has no localizing value.

A fine rapid peripheral type of vestibular nystagmus associated with gaze-paretic nystagmus in the opposite direction occurs in space occupying lesions in the cerebellopontine angle, such as acoustic neurinoma. This is called Brun's nystagmus.

Nystagmus due to Defective Convergence-Divergence Mechanism

Very rapid, small amplitude nystagmus, sustained for only a few minutes occurs in hysteria on attempting to converge the eyes.

True convergence nystagmus is characterized by rhythmic convergent movements of the eyes, exaggerated by attempts to converge or look upwards. When this nystagmus is severe, it is

associated with retraction of the eyes (nystagmus retractorius). This is usually associated with impairment of convergence and upward gaze. The nystagmus occurs because of clonic spasmodic movements of convergence with spontaneous contraction of all horizontally acting recti muscles. This condition occurs in Parinuad's syndrome.

Special Types of Nystagmoid Movements

Ocular Myoclonus

It is characterized by continuous, slow, pendular, vertical movements at the rate of one per second in one or both eyes, often associated with palatal myoclonus. The responsible lesion is usually vascular, situated in the "myoclonic triangle" Guillain Mollaret triangle in the brainstem, formed by the dentate nucleus of the cerebellum, red nucleus and inferior olivary nucleus.

Opsoclonus

These are continuous, rapid, random, chaotic, conjugate movements that persist even in sleep. These are seen in viral encephalitis, postencephalitic syndromes, and neoplasms, particularly neuroblastoma in children.

Ocular Bobbing

It is characterized by periodic, brisk, downward jerky movements of both eyes followed by slow drift upwards to the primary position. It is usually seen in comatose patients with a lesion in the pons.

Ocular Flutter

This refers to a periodic series of pendular horizontal movements when the eyes are fixing on an object. This is usually seen in diseases of the cerebellum.

Ocular Dysmetria

This is characterized by brief, nystagmoid movements when the eyes move from one target to another to refix the gaze. It is also a sign of cerebellar disease, the overshoot of the eyes occurring towards the side of the cerebellar lesion.

Square Wave Jerks

These are small (2°) horizontal jerks to either side of the midposition, associated with degenerative cerebellar disease.

Superior Oblique Myokymia

This consists of rapid, small amplitude, intermittent contractions of the superior oblique muscle of one eye, resulting in oscillopsia.

Optokinetic Nystagmus

This is a physiological nystagmus induced by a succession of rapidly moving visual targets. Normally, it can be elicited with an optokinetic drum or tape. A small drum, which is painted with black and white vertical stripes is rotated at 90 cm in front of the patient who looks at the drum. Alternately, a white tape, 90 cm long and 5 cm wide with alternating black and white squares of 5 cm is moved rapidly in front of the patient's eyes. The direction of the movement of the stimulus may be from right to left or left to right to elicit horizontal nystagmus, or from above downwards to elicit vertical nystagmus. Normal Optokinetic Nystagmus (OKN) has a slow phase and a fast phase, the slow phase will be towards the direction of movement of the object and the fast phase is in the opposite direction. Both the slow and fast phases of the nystagmus are controlled by the cerebral hemisphere towards which the stimulus moves. In case of horizontal OKN the slow phase being initiated by the occipital lobe and the fast phase by the precentral motor area of the frontal lobe. Both cerebral hemispheres take part in vertical OKN. The occipitopontine and frontopontine pathways mediate the horizontal OKN whereas frontomesencephalic pathways mediate vertical OKN.

Abnormalities in OKN help to localize the site of a cerebral lesion. In parietal lobe lesion, there will be no OKN when the stimulus is moved towards the side of the lesion but OKN will be present when the target is moved in the opposite direction. Impairment of the slow phase of OKN will be present due to a lesion in the occipitopontine pathway while absence of fast phase will be seen with lesion in the frontopontine pathway. While testing for vertical OKN, if the fast phase is absent, it indicates bilateral lesions of the frontomesencephalic pathways.

In vestibular lesions, the jerk nystagmus will be potentiated if the stimulus for OKN moves towards the side of the lesion, whereas in fixation

nystagmus, either there is no change in the nystagmus or its direction reverses (inversion).

In infants and children in whom testing visual acuity by conventional methods may be difficult, normal OKN suggests that the vision is grossly normal. Normal OKN in a 'blind' person should suggest hysterical blindness.

The slow phase of optokinetic nystagmus also tests the slow pursuit movements of the eyes whereas its fast phase tests the rapid saccadic eye movements.

SUPRANUCLEAR MECHANISM OF EYE MOVEMENTS

For normal vision, in addition to the visual pathways being normal, the objects in the environment should be brought into the field of vision, both when they are stationary as well as moving in space. In order to achieve this, coordinated and symmetric movements of the eyes, brought about by the synergistic action of agonist and antagonist extraocular muscles is essential. Such movements are called conjugate movements.

Five different physiological mechanisms take part in different types of conjugate eye movements. These are:

i. Position maintenance mechanism to fix the eyes on a stationary object (ocular fixation).
ii. Pursuit mechanism, to follow or pursue a moving object.
iii. Saccadic mechanism, to bring the image of an object onto the fovea, when looking from one object to another rapidly.
iv. Convergence mechanism, to converge both eyes for near vision
v. Reflex mechanism, to maintain the position of the eyes, in relation to that of the head, body and environment, during movement.

Position Maintenance Mechanism

This mechanism is responsible to fix the eyes on a stationary object for a clear and detailed visual analysis. The pathway for this consists of fovea and the visual pathway to the striate cortex in the occipital lobes, from where impulses are transmitted by the occipitomesencephalic tract. This tract passes forwards, lateral to the lateral ventricles and medial to the optic radiation, and then through the posterior portion of the internal capsule to terminate in the pretectal and superior collicular nuclei of the midbrain and paramedian reticular formation in the pons (PPRF) on the opposite side, mostly crossing at the levels of III and IV nerve nuclei.

Tests: Ask the patient to look steadily first at an object held at a distance of about 6 m and then a near one, such as his own finger held in front of his eyes. Observe the movements of his eyes. Inability to fixate and interruption of fixation are both abnormal.

Inability to fixate may be due to:

1. Disturbance of the fixation mechanism as a result of lesion in its pathway (impersistence of gaze).
2. Lack of effort.
3. Altered consciousness.

Interruption of fixation may be due to various abnormal eye movements such nystagmus and others.

Examination of ocular fixation is the first step in the examination of coordinated eye movements. If the patient is unable to maintain eye fixation, subsequent evaluation of eye movements tend to be erroneous.

Pursuit Mechanism

Pursuit movements are slow eye movements concerned with accurate tracking or following a slowly and evenly moving object in the visual field. Beyond a certain speed of movement of the object, the pursuit movements give place to saccadic movements.

The pathway for this mechanism is the same as that for fixation mechanism. The connections with pretectal and superior collicular nuclei control vertical pursuit movements and the connections with PPRF control horizontal pursuit movements. The occipital cortex on each side is responsible for the pursuit movements to the same side, whereas occipital cortex of both sides are concerned with vertical pursuit movements.

Test

Hold your finger in the patient's visual field, about 60 cm in front and move the finger slowly and steadily to the right, to the left, upwards and downwards. Instruct the patient to follow the movements of the finger. Observe the rate, range

and rhythm of the eye movements in all directions. If the visual acuity is low, use a torch instead of your finger.

Abnormalities of Pursuit Movements

a. Unilateral parieto-occipital lesion	Absence of pursuit movement to the opposite side.
b. Unilateral lesion in the occipitomesencephalic pathway	
i. Before its decussation	Absence of pursuit movement to the opposite side
ii. After its decussation	Absence of pursuit movement to the same side.
c. Bilateral lesions in the occipitomesencephalic pathway	The pursuit movements cannot be tested because of visual loss, that is usually associated with these lesions
d. Lesion in the cerebellum or its connections	Smooth pursuit movements are interrupted by saccadic movement (cogwheel pursuit)
e. Bilateral lesions of medial longitudinal fasciculus (MLF)	Absence of vertical pursuit movement along with features of bilateral internuclear ophthalmoplegia.
f. Slow velocity pursuit movements	Drugs like sedatives, tranquilizers and anticonvulsants

Saccadic Mechanism

Saccadic movements of the eyes are rapid eye movements, produced volitionally either spontaneously or on command. Once initiated, these movements continue for a definite time, i.e. till the gaze reaches the intended target and they cannot be interrupted midway. These movements also occur in the rapid eye movement phase of sleep and in the fast phase of optokinetic nystagmus and vestibular nystagmus.

The cortical center for these movements is situated diffusely in the frontal lobes, but mainly in the posterior portion of the second and third frontal gyri (area 8). The frontal cortex on each side is responsible for horizontal saccadic movement to the opposite side, whereas both frontal lobes take part in vertical saccadic movements. Fibers from these areas in the frontal cortex pass through the anterior limb of the internal capsule as frontomesencephalic tract, decussate in the midbrain and pass down to terminate in the pretectal region of the midbrain and pons and paramedian reticular formation of the pons (PPRF) of the opposite side. The connections with the pretectal nuclei control the vertical saccadic movements and the connections with the PPRF control the horizontal saccadic movements.

Test

Hold both your index fingers vertically about 60 cm in front in the same horizontal plane as the eyes, one on either side of the midline, in the midlateral position of the visual field. Instruct him to fix the gaze first on one index finger and then shift it rapidly to the other index finger, when he is asked to do so. Make him do these alternate fixation movements from one finger to the other a couple of times on command, and observe the rate, range, rhythm and promptness of initiation of these movements in either direction. Similarly keeping your fingers at a distance in the vertical plane in the midline, examine for vertical saccadic movements (Figs 32.13A and B).

Abnormalities of Saccadic Movements

a. *Unilateral frontal lobe lesion:* Impaired initiation of saccadic movements to the opposite side (oculomotor apraxia) or absence of horizontal saccadic movement to the opposite side.
b. *Unilateral parietal, superior temporal or anterior occipital lobe lesions:* Absence of horizontal saccadic movements to the side of the lesion
c. Unilateral lesion in the frontomesencephalic pathway:
 i. *Before its decussation:* Same as unilateral frontal lobe lesion. Decreased fast phase of optokinetic nystagmus and vestibular nystagmus, and gaze paretic nystagmus on gaze to the opposite side of the lesion are associated signs.
 ii. *After its decussation:* Same as above, but abnormalities are ipsilateral to the side of the lesion.





Figs 32.13A and B: Testing saccadic movements of the eye. (*See* text for description)

d. *Bilateral lesions of frontomesencephalic tracts:* Total loss of saccadic movements (global saccadic paralysis) and spasm of fixation, i.e. inability to refix ate or reverse eye fixation by saccadic movements. Loss of fast phases of optokinetic and vestibular nystagmus are associated signs.
e. *Lesions in the cerebellum and its connections:* Saccadic dysmetria (over or undershoot of the saccadic movements), and slow horizontal saccadic movements
f. *Bilateral lesions in PPRF:* Slow, vertical saccadic movements, e.g. progressive supranuclear palsy.
g. Unilateral lesion of MLF, III nerve palsy myasthenia gravis, ocular myopathy. Slow, hypometric saccadic movements.

Gaze Palsy-(UMN Type of Ophthalmoplegias)

The final common path for the horizontal conjugate eye movements lies in the PPRF which is situated anterior to the MLF, at the level of the abducent nucleus (para-abducent region). The frontomesencephalic and occipitomesencephalic tract fibers for horizontal gaze terminate in this region after decussation. Hence this region is also called pontine center for horizontal gaze. These convey excitatory impulses to the ipsilateral abducent nucleus and via the MLF to the opposite III nerve subnucleus that supplies the medial rectus muscle. Simultaneously, inhibitory impulses pass to the contralateral abducent nucleus and ipsilateral medial rectus nucleus. This results in conjugate horizontal gaze towards the side of activated pontine gaze center. The final common pathway for the vertical conjugate eye movements lies in the pretectal region of the midbrain.

Defect or dysfunction of the supranuclear control mechanisms of eye movements results in characteristic gaze palsies and abnormal saccadic or pursuit movements. The typical patterns depend on the site of the lesion. These are given below:

i. Both saccadic and pursuit movements may be affected, sometimes differentially.
ii. Both vertical and horizontal movements may be affected, sometimes differentially.
iii. Vertical gaze palsies are more common than horizontal gaze palsies.
iv. Upgaze is more often affected than downgaze.
v. Saccadic movements are involved earlier and more severely than pursuit movements.
vi. Cortical lesions usually do not produce isolated upgaze palsy whereas lesions in the midbrain can do so.
vii. Unilateral cortical lesions do not cause persistent horizontal gaze palsy, but bilateral cortical lesions can do so (Table 32.13).

Abnormalities of Gaze

a. *Combined up and downgaze palsy:* Bilateral frontal lobe lesions, e.g. Pick's disease Bilateral basal ganglia and thalamic lesions, e.g. Progressive supranuclear palsy, Huntington's chorea Midbrain midline lesions, e.g. Vascular lesion, tumors, degenerative diseases
b. *Isolated upgaze palsy:* Midbrain tectal and pretectal lesions, e.g. Vascular lesion, tumors, degenerative diseases. Forced downgaze in thalamic hemorrhage
Note: *Normal elderly individuals may have isolated restriction of upgaze.*
c. *Isolated downgaze palsy:* Midbrain lesions ventral and medial to red nucleus, e.g. Vascular lesion, degenerative disease (progressive supranuclear palsy)

Table 32.13: Differentiating features of LMN and UMN types of ophthalmoplegias

	LMN type-nuclear/infranuclear ophthalmoplegia	*UMN type-supranuclear ophthalmoplegia*
Lesion site	III, IV and VI cranial nerves or their nuclei	Cortico-mesencephalic and corticopontine pathways, basal ganglia, thalamus, brainstem
Type of palsy	Individual or combined extraocular muscle palsy	Paralysis of ocular movements or gaze palsy, the individual muscles being intact
Pupils	May be affected	Not affected
Diplopia	May be present	Absent
Squint	May be present	Absent
Reflex Movements		
I. Oculocephalic reflex	Absent	Preserved
II. Oculovestibular reflex	Absent	Preserved

d. *Horizontal gaze palsy:*
 i. To the hemiplegic side Frontal lobe, thalamus or midbrain lesion, contralateral to the hemiplegic side
 ii. To the normal side
 Pontine lesion (PPRF), contralateral to hemiplegic side.

Convergence Mechanism

This mechanism is responsible for the convergence of both eyes for near vision. The cortical center for the convergence movement is located in the occipital cortex, from where fibers pass forward through the occipito-mesencephalic tract to the pretectal area in the midbrain to terminate on the oculomotor nuclei that innervate the medial recti muscles. Fronto-mesencephalic pathways also mediate this movement on volition.

Test

Ask the patient to look at a distant object and then at your finger, held in the midline, 10 centimeters in front of the nose. Observe for the smooth and equal turning of the eyes downwards and inwards and also for pupillary constriction.

Note: Do not use a light source in the place of finger as a target, because light evokes pupillary constriction as a part of light reflex. Hold the target at and not below the level of the eyes, so that you can observe the pupils unobstructed by the upper lids.

Reflex Mechanism

Eye movements occur reflexly in response to impulses coming from the vestibular apparatus and proprioceptive receptors of neck muscles. The afferent impulses from these structures reach their respective centers or nuclei in the pons and medulla, where the medial longitudinal fasciculus (MLF) connects these areas to PPRF and nuclei of III, IV and VI cranial nerves.

Tests

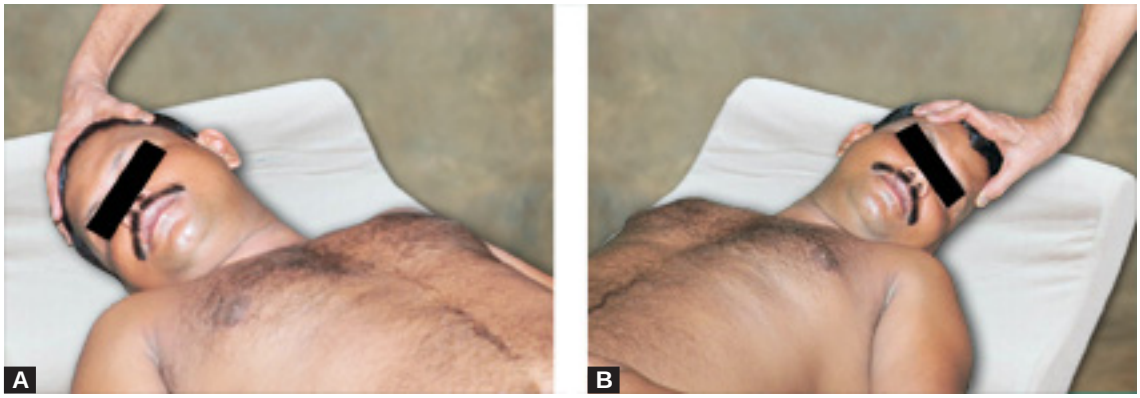
Oculovestibular reflex (OVR): This is tested by irrigating the external auditory canals with cold (30° C) and warm (44° C) water. Hence, it is also called 'caloric' test. Warm caloric stimulation is generally a greater stimulus than cold, unless the water is ice cold. For the method of testing and normal response (See chapter 53).

The afferent pathway for this reflex is through the vestibular nerve to the vestibular nuclei which are connected to the III, IV and VI nuclei through the MLF. The efferent pathway is through these cranial nerves to the extraocular muscles.

Presence of normal response on both sides indicates that the reflex arc is intact, both peripherally and centrally in the brainstem. Absence of normal response on both sides suggests a brainstem lesion or damage to the peripheral components of the reflex arc bilaterally. Absence of normal response on one side suggests unilateral brainstem lesion. In a comatose patient, if the response is absent, it indicates extensive structural damage to the brainstem or severe brainstem dysfunction.

Oculocephalic reflex (OCR): The eyeballs reflexly deviate to the side opposite to that of passive movement of the head under certain pathological conditions. Abnormalities of this oculocephalic reflex give clues to the site of lesion. Hence, these are important.

Horizontal movements of the eye are elicited by turning the head passively from side to side



Figs 32.14A and B: Eliciting doll's eye movements—description in text

and vertical movements of the eye, by bending and extending the neck.

Test: Hold the patient's head with both hands, keeping his eyelids open with your thumbs. If he is conscious, ask him to fixate his gaze on any object of interest. Turn his head passively and rapidly from side to side through a range of about 70ºC Observe the movements of his eyes.

If the eyes move in a direction opposite to hat of the head, it is called doll's eye response, since it resembles that seen in children's dolls. Presence of doll's eye response in both directions in a conscious patient with gaze palsy, indicates that the nuclear and infranuclear pathways for this reflex are intact and the conjugated gaze palsy is due to a supranuclear lesion (Figs 32.14A and B). Absence of this response suggests that the cause of palsy is at the nuclear or infranuclear level. Complete absence of doll's eye response or dysconjugate movements of the eyes in a comatose patient suggests extensive structural damage to the brainstem or severe brains-term dysfunction. However, in drug-induced coma, doll's eye response will be preserved. Normal awake individuals do not show doll's eye response.

TRIGEMINAL NERVE—V CRANIAL NERVE

Applied Anatomy

The trigeminal nerve, the largest of all cranial nerves, has both sensory and motor components. It is attached to the anterior aspect of the pons near its upper border by a large sensory root and a small motor root. The sensory root is formed by the central processes of the neurons in the gasserian ganglion which is situated on the petrous bone in the middle cranial fossa. The peripheral processes of the neurons in the ganglion group together to form 3 divisions, ophthalmic or first division: maxillary or second division and mandibular or third division.

The ophthalmic division supplies the skin over the forehead, upper eyelid and its conjuctival surface, greater part of the cornea, bulbar conjuctiva, skin over the bridge of the nose, anterior portion of the scalp up to the vertex and the lacrimal gland. After passing through the cavernous sinus and the cerebellopontine angle, it enters the orbit through the superior orbital fissure. The maxillary division supplies the skin over the cheek, anterior part of the temple, lateral aspect of the nose, lower eyelid and its conjunctival surface, upper lip, and the mucous membrane of the nose, upper part of the pharynx, roof of the mouth, part of the soft palate, and the tonsils. The lower portion of the cornea, especially on the nasal side is also supplied by the maxillary division. The maxillary division leaves the cranial cavity through the foramen rotundum, enters the orbit through the inferior orbital fissure, passes in the inferior orbital groove and exits into the face through the inferior orbital foramen.

The mandibular division is the largest and it carries both sensory and motor fibers. It supplies the skin over the lower jaw, lower teeth, skin over the anterior surface of pinna of the ear, anterior part of the external auditory meatus, anterior 2/3 of tongue, floor of the mouth and buccal surface of the cheeks. It also innervates eight muscles and supplies secretomotor fibers to submandibular and sublingual salivary glands.

Trigeminal nerve has four nuclei—the main sensory nucleus, the spinal nucleus, the mesencephalic

nucleus and the motor nucleus. The main sensory nucleus is situated in the posterior part of the pons and is continuous below with the spinal nucleus. The spinal nucleus extends from the pons down through the whole length of the medulla oblongata and into the spinal cord as far as the second cervical segment. The mesencephalic nucleus is situated in the lateral part of the grey matter around the cerebral aqueduct in the midbrain and extends inferiorly into the pons as far as the main sensory nucleus. The motor nucleus is situated in the pons, medial to the main sensory nucleus.

Sensory Component of the Trigeminal Nerve

The sensations of touch, pressure, pain, temperature and proprioception from the face are carried by axons in the three peripheral divisions of the trigeminal nerve whose cell bodies are situated in the Gasserian ganglion. The central processes of these cells form the sensory root of the trigeminal nerve. After reaching the pons, most of these fibers divide into small ascending branches and long descending branches, while the rest either ascend or descend without branching. The ascending branches carry the sensations of touch and pressure and they terminate in the main sensory nucleus. The descending branches carry the sensations of pain and temperature and they terminate in the spinal nucleus. The axons of the unipolar neurons of the mesencephalic nucleus bypass the gasserian ganglion and these carry proprioceptive impulses from the muscles of mastication and from the facial and extraocular muscles.

It is important to note the disposition of the sensory fibers. Those from the ophthalmic division are situated most ventrally in the spinal tract and they terminate in the lowermost part of the spinal nucleus. Fibers from the maxillary division occupy intermediate position in the spinal tract and terminate in the middle part of the spinal nucleus. Those from the mandibular division are most dorsal in the spinal tract and terminate in the upper part of the spinal nucleus. In other words the face is represented in an upside down manner in the spinal nucleus.

The axons of second order neurons in the spinal nucleus cross the midline to the opposite side and ascend along with the medial lemniscus to terminate in the ventral posteromedial (VPM) nucleus of the thalamus. The axons of the second order neurons in the main sensory nucleus are both crossed and uncrossed and they also terminate in the VPM nucleus of the thalamus. The central connections of the mesencephalic nucleus are not well established but probably they project to the cerebellum. From the VPM nucleus of the thalamus, the thalamocortical fibers travel through the internal capsule to the lower part of the postcentral gyrus of the cerebral cortex.

Motor Component of the Trigeminal Nerve

The motor nucleus of the trigeminal nerve supplies the muscles of mastication (temporalis, masseter, the medial and lateral pterygoid muscles), the tensor tympani, tensor veli palatini, mylohyoid and anterior belly of the digastric. The motor nucleus receives corticonuclear fibers from both cerebral hemispheres, fibers from the reticular formation, the red nucleus, the tectum, medial longitudinal fasciculus and from the mesencephalic nucleus.

Some secondary trigeminal fibers, both crossed and uncrossed, establish reflex connections between the muscles of mastication, skin of the face and mucous membranes of the tongue, mouth and nasal cavities.

Trigeminal Reflexes

Secondary trigeminal fibers ascending and descending in the brainstem give off collaterals to various motor cranial nerve nuclei. These connections are involved in a large number of reflexes. Of these, the corneal reflex and jaw jerk are clinically most important.

i. *Corneal reflex:* Touching the cornea with a wisp of cotton results in bilateral blinking and closure of the eyes. The afferent pathway is through the ophthalmic division of the trigeminal nerve on the stimulated side, the center is in the pons and the efferent pathway is through the facial nerves on both sides. The secondary trigeminal fibers from one side project bilaterally to the facial nuclei.
ii. Jaw jerk (See Table 32.17 on page 456) Fig. 32.15.
iii. *Tearing reflex:* This is mediated by the secondary trigeminal connections with the superior salivary nucleus of the facial nerve.

This leads to secretion of tears in response to intensive stimulation of mucous membrane of the mouth or nose.

iv. *Sneezing reflex:* This is mediated by the secondary trigeminal connections with the nucleus ambiguous, respiratory centers in the brainstem, phrenic nerve nuclei and anterior horn cells innervating intercostal muscles in the spinal cord. Stimulation of the mucous membrane of the nose leads to sneezing.

v. *Vomiting reflex:* This is mediated through the connections of the trigeminal nuclei to the vagal nuclei.

vi. *Salivary reflex:* This is mediated through the connections of the trigeminal nuclei to the salivatory nuclei. Stimulation of the oral mucosa leads to salivation.



Fig. 32.15: Jaw jerk. Strike over the chin with mouth half open elicits reflex contraction of the muscles of mastication and the jaw closes. V nerve is both afferent and efferent

Tests

1. *Tests for sensory component:* Sensations of pain, temperature and touch are tested over the forehead and upper part of the side of the nose supplied by the ophthalmic division, over the cheek and the upper lip supplied by the maxillary division and over the chin and the lower jaw supplied by the mandibular division.

Note: Skin on the anterior part of the temple and the upper part of the anterior surface of the pinna of the ear is supplied by the maxillary and mandibular division respectively and not by the ophthalmic division. The skin over the angle of the jaw is supplied, not by the trigeminal nerve but by the second or third cervical root.

Tests for Motor Component (Figs 32.16A to C)

The muscles of mastication are routinely tested. Assessment of the function of other muscles supplied by the trigeminal nerve is difficult.

i. *Clenching of the jaws (masseter and temporalis muscles):* Ask the patient to clench his teeth. Inspect and palpate the contraction of the temporalis and masseter muscles on both sides. If there is paralysis on one side, the contraction of that muscle will be weak or absent on that side. However minor weakness of these muscles is difficult to detect.

ii. *Opening of the jaws* (lateral pterygoid muscles): Ask the patient to open his mouth widely, but slowly.



Figs 32.16A to C: Palpating contractions (A) Temporalis, (B) Masseter, (C) movement of the jaw by pterygoids

Normally, the chin should move downwards in the midline. Deviation to either side indicates weakness of the lateral pterygoid of the side to which the chin deviates. While opening the mouth the lateral pteygoid muscle pushes the jaw to the opposite side and balanced action of both these muscles keep the jaw in the midline.

Minor deviation of the jaw can be detected by comparing the relative positions of the middle of the chin and the upper central incisor teeth which should all be in the same line.

The strength of the lateral pterygoid muscles can also be assessed by asking the patient to open his mouth while applying resistance to the chin from below.

iii. *Side to side movement of the jaw* (lateral and medial pterygoid muscles): Ask the patient to move his lower jaw from side to side, against resistance. In unilateral paralysis of the pterygoid muscles, the movement of the jaw to the opposite side will be weak or absent.

iv. *Size, contour and fasciculations of the muscles:* Hollowing and diminished size of the temporalis and masseter muscles can be detected above and below the zygoma, due to wasting of these muscles. Sometimes, fasciculations can be observed in these muscles.

v. Paralysis of the tensor tympani may be detected as partial deafness to low pitched sounds by suitable investigations. Weakness or paralysis in the tensor veli palatini may be recognized as mild palatal weakness at times.

iv. Inability to close the mouth by actively elevating the lower jaw and the resultant jaw drop suggests bilateral paralysis of the muscles of mastication.

Testing Corneal Reflex

Touch the lateral edge of the cornea quickly but gently with a wisp of clean cotton wool and note the response. Normally both eyes should blink promptly. Contraction of the ipsilateral orbicularis oculi is the direct reflex and that of the contralateral muscle is the consensual reflex. In unilateral lesion of the fifth nerve, on touching the ipsilateral cornea, there will be no blinking on either side, but consensual reflex will be present when the cornea on the opposite side is stimulated. In unilateral facial nerve palsy, the paralyzed side does not blink but the eye on normal side does so on stimulating the cornea of either side.

Note:

i. Touch both upper and lower parts of the cornea while testing the corneal reflex because at times the lower part of cornea may be supplied by the maxillary division.

ii. Bring the wisp of cotton from the lateral side and not from the front to avoid defensive eye blinking even before the cornea is touched.

iii. Do not wipe or rub the corneal surface with the cotton wool, so as to avoid injury to the cornea.

The Conjunctival Reflex

This is elicited by touching the bulbar conjunctiva. Both corneal and conjunctival reflexes have the same pathway and clinical significance, but the former is more sensitive.

Loss of corneal reflex is an early and reliable sign of V nerve lesion. The lesion may be in the ipsilateral V nerve, Gasserian ganglion or contralateral parietal lobe. Lesions in the descending spinal tract or spinal nucleus usually do not abolish the corneal reflex.

Localization of the Lesion in Trigeminal Paralysis

Motor paralysis may be either LMN or UMN type. UMN lesion occurs due to affection of corticonuclear pathway to the motor nucleus. LMN lesions are due to affection of the motor nucleus or the mandibular nerve.

Sensory loss occurs due to lesions in the Gasserian ganglion or all or any of the three divisions.

A. Motor Paralysis

i. Unilateral UMN lesion	Mild weakness of the muscles of mastication on the opposite side, with no wasting or fasciculations. Normal corneal reflexes.
ii. Bilateral UMN lesions	Marked weakness of the muscles of mastication on both sides with no wasting or fasciculations. Exaggerated jaw jerk and normal corneal reflex.

iii.	Unilateral lesion in motor nucleus (LMN paralysis	Marked weakness, wasting and fasciculations of the muscles of mastication on the side of the lesion. Absence of jaw jerk and normal corneal reflex.
iv.	Unilateral infra nuclear lesion in the motor root or mandibular division (LMN paralysis)	Same as in nuclear lesion, but fasciculations are rare.

Sensory Loss

i.	Unilateral lesion in the main sensory nucleus	Loss of tactile sensation only over the face on the side of the lesion.
ii.	Unilateral lesion in the spinal tract or spinal nucleus	Loss of pain and temperature sensations with preservation of touch, over the face on the side of the lesion
iii.	Lesion in the gasserian ganglion or its sensory root	Loss of all modalities of sensation over the face on the side of the lesion.
iv.	Lesion in the ophthalmic, maxillary or mandibular division.	Loss of all modalities of sensations in the distribution of the affected division.

Note: Lesions in cerebellopontine angle region (e.g. acoustic neurinoma) involve the ophthalmic division of trigeminal nerve along with VII and VIII cranial nerves on the same side. Lesions in the cavernous sinus (e.g. cavernous sinus thrombosis) usually involve the ophthalmic division along with III, IV and VI cranial nerves on the same side. Lesions in the superior orbital fissure (e.g. Tolosa Hunt syndrome) involve the ophthahnic division along with III, IV or VI cranial nerves on the same side. Optic nerve may be occasionally involved.

FACIAL NERVE—VII CRANIAL NERVE

Applied Anatomy

The facial nerve is a mixed nerve. It has 3 nuclei—the main motor nucleus, parasympathetic nucleus and sensory nucleus. The main motor nucleus is situated deep in the pons. That part of the nucleus which supplies the muscles of the lower part of the face receives corticonuclear fibers only from the contralateral cerebral hemisphere, whereas that part of the nucleus which supplies the muscles of the upper part of the face receives corticonuclear fibers from both cerebral hemispheres. This accounts for the fact that in unilateral upper motor neuron (UMN) type of facial palsy only the lower part of the face is affected on the opposite side. The superior salivatory and lacrimal nuclei, which are parasympathetic, lie posterolateral to the motor nucleus. The sensory nucleus is the upper part of the nucleus of the tractus solitarius and lies close to the motor nucleus. Sensation of taste from the anterior 2/3 of the tongue travels through the chorda tympani to the sensory nucleus. The fibers from the facial nucleus wind round the abducent nucleus in the pons and emerge from the brainstem at the junction between the pons and the medulla. In lesions of the pons, these two nuclei are often affected together.

After its emergence from the brainstem the facial nerve travels through the middle cranial fossa and enters the petrous temporal bone through the internal auditory meatus. The nerve then passes through the facial canal in the temporal bone. Within this canal it gives off a branch to stapedius muscle and distal to that branch the chorda tympani leaves the facial nerve to join the lingual nerve. In the petrous temporal bone the nerve makes a sharp bend (genu) where the geniculate ganglion is situated. In the facial canal it lies in close relationship to the medial wall of the middle ear. This relationship makes the nerve vulnerable to damage in lesions of the middle ear. The nerve leaves the temporal bone through the stylomastoid foramen and traverses through the parotid gland to divide into terminal branches that supply all the muscles of facial expression, auricular muscles, posterior belly of the diagastric and stylohyoid muscle.

The sensory nucleus receives taste fibers from the anterior 2/3 of the tongue, the floor of the mouth and the soft palate. Facial nerve carries general sensations from the external auditory canal, tympanic membrane, lateral surface of pinna, a small area behind the ear and skin over the mastoid process. It also carries proprioceptive sensations from the muscles it supplies, deep pain, and

pressure from the face. However, it does not carry any superficial sensation from the face.

The superior salivary nucleus supplies the submandibular and sublingual salivary glands and the lacrymal nucleus supplies the lacrymal gland.

Tests for the Facial Nerve

Motor Part

Muscles of facial expression, orbicularis oculi, frontal belly of occipitofrontalis, buccinator, orbicularis oris, mentalis and platysma can be tested separately.

1. Observe the patient's face for any abnormality or asymmetry between the two sides when he is at rest and when he is talking, smiling and blinking. In facial palsy the face on the affected side will be flatter, nasolabial fold is obliterated and angle of the mouth is at a lower level due to paralysis of levator anguli oris. The mouth appears to be pulled towards the normal side. The lower eyelid sags down from the eyeball and this leads to epiphora. Blinking on the affected side will be absent or weak and the palpebral fissure cannot be closed full due to paralysis of orbicularis oculi. The normal wrinkles on the forehead are abolished due to paralysis of frontal belly of occipitofrontalis. When he attempts to smile or talk, the muscles on the normal side draw the angle of the mouth towards the normal side. When he attempts to hold water in his mouth or spit, the water escapes from the affected side quite unexpectedly due to paralysis of buccinator. In many cases this is the presenting complaint.
2. Ask him to wrinkle his forehead and observe the rate and range of the movement of the two eyebrows. Normally, both sides move up with equal wrinkling. In LMN facial palsy, the affected side does not move upwards due to paralysis of frontal belly of occipitofrontalis.
3. Ask him to close his eyes tightly against resistance. This is the test for orbicularis oculi. In LMN facial paralysis the eye on the affected side cannot be closed tightly, and it can be easily opened passively. On attempted closure of the eyes, the eyeball rolls up prominently Bell's sign.
4. Ask the patient to retract the corners of the mouth laterally as if to show the teeth, in order to test the levator anguli oris muscles. In facial palsy, the angle of the mouth on the affected side will not move as much as the normal side.
5. Ask him to purse his lips tightly against resistance. This tests power of orbicularis oris muscle.
6. Ask him to blowout his cheeks keeping his mouth closed. Tap or press with your finger on the inflated cheek, first on one side and then on the other. Normally air should not escape through pursed lips. Escape of air on one side points to weakness of the buccinator muscle. Weakness of buccinator also leads to collection of food material between the cheek and teeth on the affected side during eating (Figs 32.17 and 32.18).
7. Ask him to clench his teeth and simultaneously attempt to depress the corners of the mouth downwards as if he is grimacing. This tests contraction of the platysma muscle. Longitudinal folds of skin become visible in the neck when the muscle contracts.

Taste Sensation

In LMN facial palsy due to lesions occurring near the geniculate ganglion, taste from the ipsilateral half of anterior 2/3 of the tongue is abolished. Ask the patient to protrude his tongue. Wrap the tip of the tongue with a gauze piece or tissue paper and hold it gently between your left index finger and thumb. Dry the tongue surface with gauze. Place damp granules of sugar on one side of the tongue (anterior part) and ask him to indicate by gesture or writing whether he is able to taste the substance correctly. After testing with sugar, rinse his mouth with water and repeat the test with salt, quinine for bitter, and vinegar for sour taste.

Inability to identify correctly or delay in his response is abnormal. Use of solutions may lead to erroneous responses because of spread to the normal side. Abnormalities of taste may be

- Ageusia: loss of taste sensation
- Hypogeusia: reduced sensation of taste
- Parageusia: perverted taste sensation.

Facial Reflexes

1. Corneal and conjunctival reflexes (*See* page 432)
2. Sucking reflex (*See* page 463)
3. Palmomental reflex (*See* page 463)
4. Orbicularis oculi reflex (glabellar reflex): Percussion over the root of the nose causes closure of the eyes on both sides. Afferent path is through



Figs 32.17A and B: Testing the superficial muscles of the face
(A) Frontalis, (B) Orbicularis oculi (arrow) and orbicularis oris (star)



Figs 32.18A and B: Testing superfacial muscles of the face (A) Levators anguli oris, (B) Buccinator

trigeminal nerves, center is in the pons and efferent is through the facial nerves. It is absent in LMN facial paralysis and is exaggerated in UMN facial paralysis. It is also exaggerated and persistent in parkinsonism (Fig. 32.19).

5. Palpebral-oculogyric reflex (Bell's phenomenon) Normally, while attempting to close the eyes, the eyeballs roll up reflexly equally on both sides. The afferent is through the proprioceptic fibers of the facial nerve and the center is the portion of the third cranial nerve nucleus supplying the superior rectus, levator palpebrae superioris and inferior oblique muscles which are the effectors. This response is exaggerated on the side of LMN facial palsy so that the whole cornea goes under the upper eyelid. This exaggerated response is called Bell's phenomenon. In UMN type of facial palsy, Bell's phenomenon does not occur.
6. Orbicularis oris reflex(Snout reflex): Normally, percussion with a finger over the lateral part of the upper lip or by the side of the nostril results in elevation of the upper lip and angle of the mouth. V nerve is the afferent and VII, the efferent. This reflex is exaggerated in UMN type of facial palsy and also in extrapyramidal disorders. If both the upper and lower lips protrude, it is called "snout" reflex, which occurs in bilateral UMN type of facial paralysis and some cases of dementia (Fig. 32.20).



Fig. 32.19: Orbicularis oculi reflex (glabellar reflex) (*see* text for description page 463)



Fig. 32.20: Snout reflex (*See* text for description also refer to the page primitive reflexes page 463)

Types of Facial Paralysis

The lesion in the facial nerve pathway may be either in

i. its nucleus,
ii. in the peripheral portion of the nerve, or
iii. in its corticonuclear connections. Nuclear and nerve lesions cause LMN paralysis. Supranuclear (corticonuclear) lesions cause UMN paralysis. Features that distinguish these two types are given in Table 32.14.

LMN Type of Facial Paralysis

A. *Nuclear lesion:* Lesions in the pons may affect the nucleus of facial nerve. They are almost always accompanied by other cranial nerve palsies especially the sixth. Long tract signs-both motor and sensory are present on the opposite side, leading to crossed hemiplegia. The common causes are infarction, hemorrhage, demyelinating diseases and tumors occurring in the pons.

B. *Infranuclear lesions*

i. Involvement of the facial nerve after its emergence from the pons and before it enters the facial canal in the petrous temporal bone is usually due to lesions in the cerebello- pontine angle. In such cases the facial palsy is associated with affection of VIII, ophthalmic division of V and other lower cranial nerves on that side (Table 32.15). Cerebellar signs may also be present. The common lesions are acoustic neurinoma, cysts, metastatic deposits and abscess in the cerebellopontine angle region.

ii. Involvement of the nerve within the petrous temporal bone. The facial nerve is affected in its intrapetrous course by lesions such as fractures, osteomyelitis, otitis media and metastatic deposits.

Table 32.14: Showing the distinguishing features of LMN and UMN type of facial palsy

Clinical features	*LMN lesion*	*UMN lesion*
Degree of weakness	Usually dense paralysis	Usually partial paresis
Extent of paralysis	Both upper and lower part of face on the side of lesion	Only lower part of face, contralateral to the side of lesion
Watering from the eye	Present	May not be present
Voluntary movements of facial muscles	Lost	Lost
Emotional movements of facial muscles	Lost	Preserved and even exaggerated
Taste sensation in the anterior 2/3 of the ipsilateral half of the tongue	Lost in lesions proximal to geniculate ganglion	Present
Corneal reflex Glabellar reflex Orbicularis oris reflex Bell's phenomenon	Lost Absent Absent Present	Usually preserved Exaggerated Exaggerated Absent
Common association	LMN palsy of other cranial nerves	Often this is part of hemiplegia

Table 32.15: Clinical features of different sites of lesions in the facial canal

	LMN facial palsy	*Loss of taste in anterior 2/3rd of tongue*	*Hyperacusis*
* Lesion between internal auditory meatus and geniculate ganglion	+	+	–
Lesion at or just proximal to geniculate ganglion	+	+	+
$ Lesion between nerve to stapedius and ganglion of facial nerve	+	+	+
Lesion between chorda tympani and nerve to stapedius	+	+	–
Lesion at stylom astoid foramen	+	–	–
Lesion affecting individual branches	Partial affection	–	–

+ present, - Absent

Note: * Lesion at this site is accompanied by VIII nerve palsy which masks hyperacusis. $ This may be associated with impairment of secretion in submandibular and sublingual glands.

The most common cause of pure motor paralysis is inflammation of the nerve in the stylomastoid foramen-Bell's palsy. Figures 32.21 and 32.22. Incomplete paralysis of facial muscles occurs if the branches of the facial nerve are affected as in tumors of the parotid gland, fracture of facial bones, surgical trauma and chronic granulomas such as leprosy.

In India, leprosy is a common cause of isolated affection of one or more branches of the facial nerve. This may affect the upper branches selectively.

Upper motor neurone (UMN) type of facial palsy: This may take three forms:

i. *Volitional type:* Loss of voluntary contraction of facial muscles with preservation of mimetic movements.
ii. *Mimetic type:* Loss of involuntary contraction of facial muscles during smiling, crying, etc. (mimetic movements) with preservation of voluntary movements.
iii. *Mixed type:* Both volitional and mimetic movements are lost.

Volitional type of facial paralysis occurs in lesions of corticonuclear fibers to facial nucleus. Mimetic type of palsy occurs in lesions of basal ganglia, thalamus, hypothalamus or prefrontal lobe.

Mixed type occurs in parkinsonism leading to 'mask' like face. However, there is no true paralysis of facial muscles in parkinsonism.

Crocodile tears: In some cases of LMN facial palsy with partial recovery, whenever the patient tastes strongly flavored food, lacrymation occurs.



Fig. 32.21: Right facial palsy (LMN) showing weakness of upper part (absence of wrinkling and defect in eye closure) and weakness of lower part (deviation of angle of mouth to left) typical Bell's palsy

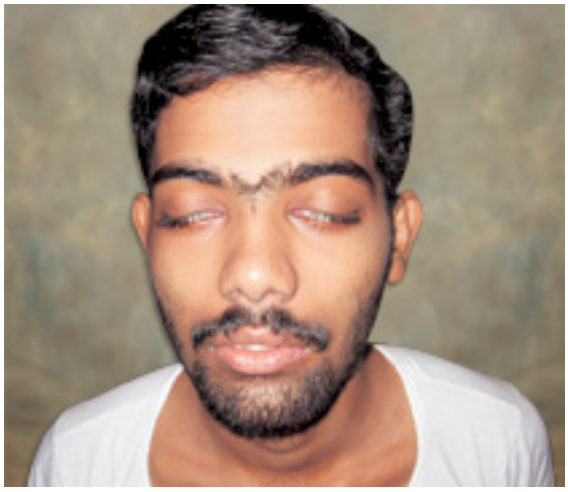


Fig. 32.22: Bilateral facial palsy occurring in Guillain-Barre Syndrome. Note the defect in eye closure and horizontal position of angles of mouth (Patient was given command to close the eyes and smile)

This is due to faulty reinnervation during recovery phase. Its presence suggests chronic LMN type of facial paresis.

VESTIBULOCOCHLEAR NERVE—VIII CRANIAL NERVE

Applied Anatomy

It is a purely sensory nerve concerned with hearing and equilibration. Vestibulocochlear or the eighth cranial nerve consists of two distinct divisions—the vestibular division which is concerned with sense of movement, position and balance and the cochlear division, concerned with hearing.

The vestibular nerve fibers arise from the utricle, saccule and the semicircular canals in the internal ear, pass proximally in the vestibulo cochlear nerve through the cerebellopontine angle and enter the brainstem at the pontomedullary junction. There they end in the vestibular nuclear complex consisting of four nuclei superior, inferior, medial and lateral vestibular nuclei. The vestibular nuclei have connections with the cerebellum; III, IV and VI cranial nerve nuclei through medial longitudinal fasciculus (MLF) and with the spinal cord through the vestibulospinal tract.

The fibers of the cochlear nerve arise from the spiral ganglion of the cochlea in the internal ear; pass proximally in the vestibulocochlear nerve through the cerebellopontine angle and enter the brainstem, to terminate in the anterior (ventral) and posterior (dorsal) cochlear nuclei situated on the surface of the inferior cerebellar peduncle. The fibers from these cochlear nuclei pass medially in the pons to end in the trapezoid bodies of the ipsilateral and contralateral sides. The fibers from the trapezoid body ascend up into the midbrain as the lateral lemniscus which partly terminates in the nucleus of the inferior colliculus and partly in the medial geniculate body. Fibers from these pass to the auditory cortex of the superior temporal gyrus on both sides through the acoustic radiation in the internal capsule.

Tests for the Cochlear Nerve

Whispering Test

Ask the patient to stand at 6 m distance with the ear to be tested facing towards you. Ask him to plug the other ear with his finger. Whisper a series of numbers or letters and ask him to repeat the same as you whisper. Give ten such numbers or letters. Repeat the test on the opposite side by turning the patient so that the other ear to be tested faces towards you. If hearing is normal, the person should be able to repeat at least 9 out of 10 letters or numbers. Whispering test cannot differentiate conduction deafness from nerve deafness. Similarly, a conversational voice should normally be heard at 3.5 m.

Tuning Fork Test

The tuning fork helps not only to detect deafness but also to differentiate conduction deafness from nerve deafness. Tuning fork with a frequency of 256Hz and above is used.

a. *Rinne's test:* Place the base of the vibrating tuning fork on the mastoid process of the patient. The sound will be heard by the patient through bone conduction. Ask him to indicate when he stops hearing the sound. As soon as he indicates this, quickly bring the limbs of the tuning fork near to the external auditory meatus and enquire whether he is still hearing the sound. This tests hearing through air conduction. A person with normal hearing will be able to hear the sound by air conduction even after hearing by bone conduction has stopped. This is described as 'Rinne positive'. If the bone conduction is found to be better than the air conduction, it indicates middle ear disease or conduction deafness in that ear. This is described as 'Rinne negative'. In nerve deafness, the Rinne test will be positive.

b. *Weber's test:* Place the base of the vibrating tuning fork over the vertex of the patient's head and ask him to indicate whether he is hearing the sound equally on both sides or only in one ear. Normally, the sound will be heard equally on both sides so that the patient will feel that the sound is coming from the forehead. If there is conduction deafness in one ear, the sound will be better heard in that ear. If there is nerve deafness in one ear, the sound will be heard in the opposite normal ear. This is described as lateralization of Weber test. Loss of hearing df low tones suggests nerve deafness. Total hearing loss occurs only in nerve deafness. *See* also Chapter 52 for further details.

GLOSSOPHARYNGEAL NERVE—IX CRANIAL NERVE

Applied Anatomy

The glossopharyngeal or the ninth cranial nerve is both sensory and motor. It has 3 nuclei—the main motor nucleus, the parasympathetic nucleus and the sensory nucleus. The main motor nucleus is situated in the medulla oblongata and is formed by the upper end of the nucleus ambiguous. It receives corticonuclear fibers from both cerebral hemispheres and supplies stylopharyngeus muscle. The parasympathetic nucleus, also called the inferior salivary nucleus, receives afferent fibers from the hypothalamus, olfactory system and nucleus of the tractus solitarius. The postganglionic fibers supply the secretory fibers to parotid gland through the otic ganglion. The sensory nucleus is a part of the nucleus of the tractus solitarius and it receives nerve fibers from tympanic cavity, tonsils, posterior part of the soft palate, posterior third of the tongue and the pharynx. Sensation of taste from the posterior third of the tongue is also carried by this nerve. The central processes of these cells pass to the opposite thalamus from where they are projected to the sensory cortex.

Stylopharyngeus muscle is the only muscle supplied and it cannot be tested individually.

Tests

Inspect the soft palate and pharynx while the patient keeps his mouth wide open. Gently touch both sides of the pharyngeal wall one after the other with a swab stick. In normal subjects, this should evoke a gag reflex, i.e. contraction of the pharynx with elevation of the root of the tongue and a feeling to vomit. Also verify whether he feels the touch sensation equally on both sides. Afferent for the gag reflex is the IX cranial nerve and efferent is the X cranial nerve. However, even in some normal individuals, gag reflex may be absent. Asymmetry in the response is always abnormal.

Sense of taste in the posterior 1/3 of the tongue is tested as in the case of anterior 2/3, but it is technically more difficult. An alternate method is to apply a weak electric current to the back of the tongue. Normally, this evokes a sour taste.

Glossopharyngeal neuralgia is a disorder of the IX cranial nerve characterized by lancinating pain felt episodically at the back of the throat but on clinical examination the nerve normal.

VAGUS NERVE—X CRANIAL NERVE

Applied Anatomy

Vagus nerve is a mixed nerve. It arises from the side of the medulla oblongata below the IX nerve by several filaments which join together, run in the posterior cranial fossa and leave through the jugular foramen along with the IX and XI cranial nerves.

Its motor supply is to the muscles of the palate, pharynx and larynx and sensory supply is to external ear, pharynx, larynx, trachea, esophagus, thoracic and abdominal viscera and the dura mater of the posterior fossa. It supplies parasympathetic fibers to the thoracic and abdominal viscera.

Nucleus of the vagus nerve is situated in the medulla oblongata in the floor of the fourth ventricle. The dorsal nucleus is a mixed nucleus and the motor fibers arising from it go to the involuntary muscles of bronchi, heart, esophagus, stomach and the intestines. The motor fibers which arise from nucleus ambiguous in the medulla innervate the various muscles in the pharynx and larynx. The sensory fibers which terminate in the dorsal nucleus are derived from larynx, pharynx, lungs, heart, esophagus, stomach and the intestines. Taste sensation from taste buds in the epiglottis and vallecula reaches the nucleus of tractus solitarius. Bedside examination of vagus nerve consists of the examination of palate, pharynx, larynx and vocal cords.

Tests for Vagus Nerve

Motor Function

a. *Palate:* Observe the arches of the palate on both sides with the patient holding his mouth wide open. Normally, both sides should be symmetrical. In unilateral palatal paralysis the arch on that side will be at a lower level.
 Ask the patient to say 'ah' and observe the movements of the palate. Normally, both the arches will lift up to the same extent and the base of the uvula will be moving up in the



Fig. 32.23: Movement of the soft palate on saying 'ah'. Note the uvula moving in the midline in normals (arrow)

midline (Fig. 32.23). In unilateral palatal paralysis only the normal side will rise up while the paralyzed side will remain lower and immobile. The midline raphe of the palate and the base of the uvula will be pulled towards the normal side. The gag reflex will be diminished on the side of paralysis (Figure movement of the palate)

b. *Pharynx:* Observe the speech of the patient. In pharyngeal paralysis it will have a bubbling character because of pooling of saliva in the pharynx. Speech will have a nasal quality. Swallowing: In pharyngeal paralysis, the patient will have difficulty in swallowing. There will be pooling of secretions in the pharynx. Ask the patient to swallow a mouthful of water in the sitting position. In palatal paralysis, fluid regurgitates through the nose, since the palate fails to close the nasopharynx.

 Note: In patients who have severe paralysis of the vagus and in those who are semi-conscious, swallowing may lead to aspiration of food into the trachea. In case of unilateral pharyngeal paralysis, the symptoms will be mild whereas in bilateral paralysis, the symptoms of dysphagia and bubbling speech will be marked and the patient may develop coughing and choking when he attempts to swallow fluids.

c. *Larynx:* The voice becomes hoarse in paralysis of the vocal cords (dysphonia). In bilateral abductor paralysis the vocal cords come to the midline obstructing the airway. This is fatal. In total paralysis of all muscles, the vocal cords occupy the cadaveric position, i.e. midway between abduction and adduction. Since the vocal cords cannot move and close the glottis during coughing, the tussive phase of cough reflex is abolished, i.e. when the patient is asked to cough the explosive phase is absent. This is called bovine cough. In unilateral paralysis, with the passage of time (weeks or months), the vocal cord on the normal side crosses the midline to lie near its fellow and thereby restores the vocal aperture. Hence in chronic vocal cord paralysis cough may regain its quality.

Since patients with paralysis of the vocal cords cannot close the glottis and hold the breath, they run the risk of drowning if immersed in water. Movement of the vocal cords can be inspected by direct and indirect laryngoscopy.

ACCESSORY NERVE—XI CRANIAL NERVE

Applied Anatomy

The eleventh cranial nerve is a motor nerve. It has a cranial component originating from nucleus ambiguous in the medulla and a spinal component arising from the anterior horn cells of the upper five cervical spinal segments.

The spinal portion emerges from the cord between the anterior and posterior roots and forms a trunk which ascends up to the foramen magnum where it is joined by the cranial accessory portion. The common trunk leaves the cranial cavity through the jugular foramen, along with the vagus and glossopharyngeal nerves and travels down in the neck. Fibers of the cranial root are distributed along with the pharyngeal and recurrent laryngeal branches of the vagus. These are motor nerves. Fibers of the spinal root supply the sternomastoid and trapezius muscles.

Test for Sternomastoid Muscle

Ask the patient to turn his head to one side while applying resistance to the chin. This movement is mediated by the sternomastoid of the opposite side which can be seen to contract actively. Its strength can also be assessed objectively and compared with the opposite side. Observe for wasting and fasciculations (Fig. 32.24).



Fig. 32.24: Test for action of stemomastoid. Note the contracted muscle (arrow *see* text for description)



Fig. 32.25: Tests for trapezius muscles (*See* text for description)

Test for Trapezius Muscle

Stand behind the patient and observe the bulk and symmetry of the muscle on both sides. Ask the patient to lift his shoulders up against resistance applied on his shoulders and compare the strength on both sides (Fig. 32.25).

Upper motor neuron lesions of the sternomastoid and trapezius muscles produce only slight weakness. In bulbar palsy, along with other bulbar nerves, accessory, nerve also may be affected leading to bilateral LMN palsy. The spinal accessory nerve may be affected by compression at jugular foramen.

HYPOGLOSSAL NERVE—XII CRANIAL NERVE

Applied Anatomy

The hypoglossal nerve is a motor nerve that arises from the hypoglossal nucleus in the lower part of the medulla oblongata and passes through the anterior condylar foramen at the base of the skull to enter the oral cavity. It supplies all the intrinsic muscles of the tongue—the hyoglossus, styloglossus, and genioglossus muscles of the same side. These muscles acting from the hyoid bone protrude the tongue in the midline and take part in bending and twisting movements of the tongue required for mastication, deglutition and speech.

Tests

1. *Protrusion of the tongue:* Ask the patient to open his mouth and put out his tongue. Normally the tongue protrudes in the midline due to balanced action of its muscles. If there is paresis or paralysis of one side, the tongue deviates towards the affected side, because of the unopposed contraction of the muscles of the opposite side (Fig. 32.26).
2. *Lateral movements of the tongue:* Ask the patient to move his tongue from side to side and note the rate and range of movement.

 Ask him to push out his cheeks with the tip of his tongue from within, against resistance offered by your finger from outside. Note the strength of contraction on both sides.
3. *Curling movement of tongue:* Ask the patient to curl his tongue up and down and touch his nose or lower lip with the tip of his tongue.



Fig. 32.26: Protrusion of the tongue. Note the tongue moving in the midline normally. In unilateral paralysis the tongue deviates to the paralyzed side (*See* text for description)

4. *Wasting and fasciculations:* Observe the tongue when it lies still in the floor of the mouth for its bulk, surface and involuntary movements. Longitudinal furrows on the surface of the tongue and/ or reduction in its bulk on one or both sides suggests atrophy. Small twitching movements that occur spontaneously suggest fasciculations.
5. *Tone:* Palpate the tongue when it is relaxed in the floor of the mouth. Normal tongue feels soft. If it is too soft or flabby it suggests atrophy due to LMN lesion. On the other hand, if it is firm, it suggests spasticity due to UMN lesion, Spastic tongue is small.

 Note: In the presence of unilateral facial palsy, the tongue may appear to be deviated to one side due to deviation of the angle of the mouth. In such situations observe the tip of the tongue in relation to the central incisor teeth and the tip of the nose, so as to avoid the fallacy.

LMN lesions of XII nerve produce weakness, wasting, flaccidity and fasciculations of the tongue, whereas UMN lesions produce only weakness and spasticity. In both, the symptoms will be common, i.e. dysarthria, and dysphagia. Acute unilateral paralysis gives rise to transient symptoms whereas a chronic one is usually asymptomatic. Both acute and chronic bilateral paralysis lead to pronounced abnormality.

Common Causes of Paralysis of the Lower Cranial Nerves

LMN Lesions

I. In the cranial nerve nuclei of medulla, syringobulbia, motor neuron disease, rarely poliomyelitis, tumors or vascular lesions.
II. In the course of the nerves: Intracranial portion: neurinoma arising from any of the lower four cranial nerves, meningioma in posterior fossa, epidermoid in the cerebello-pontine angle, infarction in the brainstem, basal meningitis.

Extracranial portion: neurinoma of the cranial nerves passing through the jugular foramen, tumors and enlarged lymph nodes high up in the neck, nasopharyngeal carcinoma.

UMN Lesions

Common causes include vascular lesions, tumors, demyelination in the brainstem, and motor neuron disease.

BULBAR AND PSEUDOBULBAR PALSIES

Affection of the cranial nerves arising from the medulla oblongata (bulb) or their nuclei leads to LMN paralysis and this is called bulbar palsy. UMN lesion of these cranial nerves due to a lesion in their cortical connections (corticonuclear fibers) is called pseudobulbar palsy. Usually, these lesions are bilateral. Both bulbar and pseudobulbar palsies produce the same set of symptoms dysarthria, dysphagia, dysphonia and nasal regurgitation. In addition, pseudobulbar palsy results in emotional outbursts in the form of unprovoked and uncontrolled laughing and crying. Examination of tongue in case of bulbar palsy reveals wasting and fasciculations whereas in pseudobulbar palsy it is spastic. The jaw jerk is absent in bulbar palsy whereas it is exaggerated in pseudobulbar palsy.

STANCE AND GAIT

Several neurological disorders lead to characteristic abnormalities of stance and gait. The erect posture is a highly evolved biological phenomenon, unique to man and a few other animal species. The erect posture offers considerable advantage in vision. The upper limbs are spared for other activities. Stance is the manner in which a person stands. Gait is the manner of walking or locomotion.

Stance and its Abnormalities

Stance includes the posture of the whole body, i.e. head, trunk and the extremities, when a person stands erect. Normally the person stands erect with head held up, chest is prominent forwards and the abdomen is held inwards. For maintenance of normal stance and gait, the musculoskeletal apparatus, motor pathways, proprioceptive sensations, cerebellar function, intact vestibular system, muscle tone and basal ganglia are essential. Dysfunction or abnormality in anyone of these may result in abnormal stance.

Method of Testing

Romberg's test Stance is tested by asking the patient to stand erect with feet close to each other, first with eyes open and then with eyes closed. In this position, look for unsteadiness, swaying and deviation towards any direction. Development of unsteadiness when the eyes are closed is called positive Romberg's sign (Figs 32.27A and B).

Then ask the patient to stand on one foot at a time, stand on his toes and then on his heels, both with eyes open and then closed. This helps to bring out minor abnormalities better.

Sensory Ataxia Due to Posterior Column Lesions

The term ataxia refers to imperfect control over voluntary actions. The patient is able to stand erect with eyes open, but as soon as he closes his eyes, he starts swaying from the ankles upwards. If ataxia is severe he may fall. Sometimes he attempts to stabilize himself by keeping his feet apart, so as to get a broader base. Positive Romberg's sign is suggestive of sensory ataxia due to a lesion in proprioceptive pathways, particularly the posterior columns. When the eyes are open, visual sensation helps him to maintain posture. When visual clues are removed, the person becomes unsteady and tends to fall. Sensory ataxia is seen classically in diseases affecting the posterior column such as tabes dorsalis, subacute combined degeneration of the cord and large fiber neuropathy.



Figs 32.27A and B: Romberg's test for ataxia. The patient is made to stand with feet close together and eyes open: (A) He is instructed to close the eye and maintain the same posture; (B) *See* text for further details

Cerebellar Lesions

The incoordination seen in cerebellar disease is motor ataxia. The ataxia is independent of visual mechanism. The patient is not able to stand steady even with eyes open and he sways to either side. The lesion is either in the midline structures (vermis) or in both cerebellar hemispheres. In unilateral lesions of the cerebellum and vestibular lesions, the patient tends to sway and fall to the side of lesion.

Parkinsonism

When the patient stands erect, there is flexion of head, trunk, arms and legs. This is called stooped posture.

Hemiplegia

The patient is able to stand erect with the affected upper limb adducted at shoulder and flexed at the elbow and wrist and the ipsilateral lower limb kept extended.

Lordotic Stance

In proximal myopathies the patient is able to stand erect but the lumbar lordosis is considerably exaggerated. This suggests weakness of erector spinae muscles as is seen in progressive muscular dystrophies and progressive spinal muscular atrophies.

Hysteria

The patient sways in wide arcs from his hips upwards, instead of from his ankles, but still manages to regain his balance without falling to the ground, both when the eyes are kept open or closed. This is false Romberg's sign.

GAIT AND ITS ABNORMALITIES

Examination of the gait provides clues to diagnose diseases affecting various components of the nervous system. This is a quick method to get information about the function and inter-relationship between various functional components.

A normal person walks gracefully and the following points should be noted.

The pelvis and hip on the side of leg flexion are raised and the leg sways clear of the floor, forward.

The ball of the foot and toes touch the floor gently.

The upper limbs swing in the direction opposite to the movements of the lower limbs. The trunk moves forwards and backwards with each step. These are associated movements.

Ataxic Gait

This is of two types, namely gait of sensory ataxia, due to a lesion in proprioceptive pathways and gait of cerebellar ataxia, due to a lesion in cerebellum and its connections.

Gait of sensory ataxia: If the proprioceptive deficit is mild, the gait may not be abnormal when the patient walks with eyes open but it becomes abnormal when he is asked to walk with his eyes closed. He may complain that towards evening when it becomes dark his walking becomes difficult. When the deficit is severe, even with his eyes open, the gait is irregular and jerky with a broad base. The heel touches the ground before the toes with a slapping or stamping sound. This is called stamping gait. The patient closely looks at his feet and the floor while walking, to maintain posture.

Gait of cerebellar ataxia: Abnormalities occur when the patient walks, irrespective of his visual input. In lesions of the midline cerebellar structures or vermis, the gait is staggering, unsteady, irregular and wide-based, with a tendency to sway to either side or anteroposteriorly. With unilateral cerebellar hemisphere lesions and vestibular lesions the patient tends to sway and deviate towards the affected side. When the patient is made to walk in a straight line drawn on the floor and on tandem walking, i.e. walking by placing the heel of one foot just in front of the other. The abnormalities are exaggerated and tandem walking may be impossible (Fig. 32.28).

If the patient is asked to walk around a chair in both directions, always he tends to fall towards the side of the lesion. When he is asked to walk 6 to 8 steps forwards and then backwards repeatedly with his eyes closed, he gradually turns towards the affected side (compass gait).



Fig. 32.28: Tandem walking (*See* text for description)

Spastic Gait

This is seen in upper motor neuron lesions affecting the limbs. Depending on whether the lesion is unilateral or bilateral, the gait also differs.

Hemiplegic Gait

This type of gait is seen in hemiplegia. The affected lower extremity is extended at the hip and knee, the ankle and toes are plantar flexed. The affected foot is dragged, scraping the floor by the toes. The pelvis is tilted upwards on the involved side in order to clear the foot off the ground while walking. The entire stiff lower extremity is swung around in a semicircle from the hip towards the midline. The upper extremity is adducted at the shoulder and flexed at the elbow, wrist and interphalangeal joints. The patient can turn towards the affected side and walk sideways towards the affected side more easily than towards the normal side. When the lesion is mild, the only recognizable abnormality may be dragging of the foot, shorter steps, and absence of associated movements of the upper extremity on the affected side.

Spastic Paraplegic Gait

The lower limb shows the same abnormalities as is seen in hemiplegic gait, but on both sides. In addition, in severe cases, due to spasm of adductor muscles of the thighs, the knees may cross in front of each other during walking. This is called scissors gait. The upper limbs are not involved.

Spastic Ataxic Gait

In diseases like multiple sclerosis and subacute combined degeneration of the spinal cord or any other condition where pyramidal tracts and posterior columns or peripheral nerves are affected the resultant abnormality may have features of both spastic gait and ataxic gait.

Parkinsonism Gait

Due to rigidity, bradykinesia, loss of postural reflexes and universal flexion of the body, the gait is slow and rigid with small, shuffling steps, with a tendency to fall forward-propulsion. If he walks backwards or he is pushed backwards gently he tends to fall backwards-retropulsion. As the patient walks the speed increases (festination). Normal associated swinging movements of upper limbs are abolished. If the patient is asked to turn around while walking, he turns slowly and rigidly with several short steps.

High Stepping Gait

This occurs when there is foot drop. The patient drags the foot on the ground while walking or flexes his thigh and leg more than normal in order to prevent the toes from scraping the floor. Then he flops down the foot on the floor with a characteristic sound. First the toes, then the ball of the foot and lastly the heel make contact with the floor.

High stepping gait may be unilateral or bilateral. Paralysis of tibialis anterior, extensor digitorum longus, extensor hallucis longus and peroneal group of muscles result in this abnormality. This may occur in lateral popliteal nerve palsy, peripheral neuropathy, or lesions of L4, L5 and S1 roots on segments of the spinal cord.

Waddling Gait

The patient walks with exaggerated lordosis on a broad base with exaggerated rotation of the pelvis with each step. Due to weakness of gluteal muscles the normal tilting movement of the pelvis which helps to raise the pelvis on the side of walking does not take place. Instead, the pelvis sinks towards the side of elevation of the foot. These movements of the pelvis occurring alternately, with the compensatory lateral movements of the trunk result in waddling, which is comparable to the walking of a duck. Waddling gait is seen in progressive muscular dystrophies, progressive spinal muscular atrophies and congenital dislocation of hip joints.

Frontal Ataxia or Apraxic Gait

This occurs in frontal lobe lesions even in the absence of sensory or motor deficits in the lower extremities. The patient is not able to walk normally, but he walks slowly with short, shuffling steps, dragging the feet on the ground without lifting them up. Though superficially this may resemble parkinsonism gait, the patient does not have any other feature suggestive of Parkinsonism.

Staggering or Drunken Gait

This type of gait is seen in individuals who are under the influence of alcohol or barbiturates. The affected person walks with irregular and uncertain steps, reeling and swaying in all directions with no effort on his part to correct the staggering. However, he may still be able to walk on a narrow base, and maintain his balance well, unlike the patient with cerebellar ataxia who walks on a broad base, having difficulty to maintain balance.

Hysterical Gait

The gait is bizarre and it may take any form without conforming to any of the known organic patterns. It is irregular and the pattern changes from time to time.

Examination of Motor System

Muscle Size

Assessment of muscle size enables to detect atrophy and hypertrophy of muscles. Variation in muscle size occurs in normal individuals depending on the constitutional make-up, physical activity, training and occupation. In normal subjects the muscle size will be marginally greater on the side more commonly used, depending on the handedness. A different of up to 0.5 to 1.5 cm in the circumference of the limbs at corresponding points on either side may be present normally. The size of the muscles should be assessed by inspection, palpation and measurement. If alterations in size are present, note whether they are localized to one muscle, a group of muscles, a segment or whole of a limb or the entire side of the body.

Observe particularly the muscles of face, neck, pectoral and pelvic girdles and distal parts of the extremities from behind and in front. For proper assessment, the muscles should be fully exposed. Muscle groups can be made prominent by appropriate maneuvers. Atrophy of muscles in particular locations gives rise to deformities which can be easily recognized, e.g. flattening of shoulder, claw hand, ape hand, pes cavus, claw foot, wrist drop, foot drop and others. Loss of normal rounded contour of the shoulder suggests atrophy of deltoid muscle.

Valuable additional information can be obtained by palpation of the muscles. Hypertrophied and atrophied muscles can be easily identified. Normal muscle is semi-elastic to feel. Rubbery or doughy consistency occurs in pseudohypertrophy. Atrophied muscles are soft to feel in the early stages of illness, but later when fibrosis occurs, they feel firm.

Measurement of the circumference of a limb with a tape over corresponding points in relation to a fixed bony landmark such as the olecranon process for the arm, styloid process of radius for forearm, anterior superior iliac spine for the thigh and the tip of either malleoli for the leg, should be made to detect and quantify the degree of wasting. For measurement, the exposed limbs should be kept in identical position, fully relaxed. Serial recording of measurements is the most reliable method of assess progress with treatment.

Wrist Drop

This is the failure to hold the wrist in horizontal position due to paralysis of the extensors of the wrist. This occurs in radial nerve palsy. This can be elicited by asking the patient to hold his upper limb straight in front with the forearms pronated (Fig. 32.29).

Foot Drop

This is the inability to dorsiflex the foot due to paralysis of the extensor of the foot. The lesion is in the peroneal nerve or L5 root (Fig. 32.30).

Pes Cavus

In this condition the inner arch of the foot is more concave, with drawing up of the toes. This results either due to a congenital bony deformity or due to paralysis of the intrinsic muscles of the foot innervated by the tibial nerve (L5, S1,2 spinal segments). In congenital pes cavus, deformity persists on standing up whereas pes cavus due to muscle paralysis disappears on weight bearing.



Fig. 32.29: Wrist drop, (live model). Note the dropping of the wrist. Extension of the wrist in the direction of the arrow is not possible



Fig. 32.30: Foot drop, right foot (live model). Note the dropped position of the foot and inability to dorsiflex the foot in the direction of the arrow

Claw Foot

Claw foot is characterized by dorsiflexion of the proximal phalanges of the toes, plantar flexion of the distal phalanges, foreshortening of the foot and high plantar arch. This is due to selective wasting and weakness of small muscles of the foot.

Claw Hand

This is a characteristic deformity of the hand in which the fingers are kept flexed at the interphalangeal joints and extended at the metacarpophalangeal joints. This is caused by



Fig. 32.31: Claw hand

paralysis of the dorsal and palmar interossei and lumbrical muscles. Unopposed action of flexor digitorum produces flexion at the interphalangeal joints and that of extensor digitorum produces, extension at the metacarpophalangeal joints. Typical claw hand affecting all fingers occurs in paralysis of ulnar and median nerves below the elbow. Partial clawhand affecting little and ring fingers occurs in ulnar nerve palsy at or below the elbow. In India claw hand is a common finding in neural leprosy. Sometimes, it is also seen in selective involvement of small muscles of the hand with sparing of long flexors and extensors of the fingers in progressive muscular atrophy, motor neuron disease, poliomyelitis and others (Fig. 32.31).

Simian Hand (Syn: Ape Hand)

This is a characteristic deformity of the hand in which the thumb lies in the same plane as that of other fingers and the palm. This results from paralysis of abductor pollices muscle and other thenar muscles. The common causes include median nerve palsy in the arm, progressive muscular atrophy and motor neuron disease.

Muscle Tone

Muscle tone is the resistance offered by the muscles to passive stretch. It is due to a state of partial contraction of a group of muscle fibers which contract in turn. Maintenance of tone is a primary function of the lower motor unit. It is modified by pyramidal, extrapyramidal and cerebellar influences.

Muscle tone is determined by assessing the resistance to passive movement of the limbs. The student should familiarize himself with normal tone of the limbs by observing several normal subjects. Mild changes in muscle tone may be difficult to appreciate. In disease conditions the tone may be either increased (hypertonia) or decreased (hypotonia). In hypertonia there is increased resistance to passive movement. If this increased resistance is greatest at the initial phase of the movement, and then suddenly it gives way during the later phase, it is called "clasp-knife spasticity". This is best appreciated in the flexor muscles of the upper limb and extensor muscles of the lower limb in pyramidal tract lesions.

When the resistance to passive movement is uniformly increased throughout the range of the movement, it is called 'plastic type' of rigidity, also known as 'lead pipe rigidity'. If the increased resistance is felt intermittently throughout the range of movement it is called 'cogwheel' type of rigidity. Cogwheel type of rigidity is more prominent when there is tremor in addition. Lead pipe and cogwheel types of rigidity are found in diseases of the basal ganglia, especially parkinsonism.

Spasticity is more evident in one muscle group than in the other and is more prominent in the limbs. Rigidity is felt equally in all muscle groups (agonists as well as antagonists) and is greater in the trunk, than the limbs. Repeated passive movements of the limb abolish hypertonia, due to exhaustion of the muscles.

Test for Muscle Tone

The patient should be fully relaxed and comfortable. The limb is kept free without any attempt at voluntary effort. The examiner performs the full range of movements at all joints to assess the tone. Increased tone in the flexors will give rise to resistance to passive extension and vice versa. Tone may be influenced by changes in temperature (heat depresses and cold increases), speed of passive movement, emotional state and degree of voluntary relaxation. Changes in tone can be inferred by observing the character of spontaneous movement and abnormalities of posture or position of the limbs and also by palpation of the muscles to note their consistency and firmness (Figs 32.32A and B).

Myotonic Reaction

Myotonia is a condition in which the relaxation of the muscles is slow after a strong voluntary contraction, or in response to mechanical or electrical stimulation.





Figs 32.32A and B: Testing the muscle tone (A) Passively flexing the elbow. Note the tone of the extensors; (B) Passively extending the elbow. Note the tone of the flexors *(See* text for description)

Test

Grasp Myotonia

Ask the patient to grasp your hand or finger firmly for about 5 seconds and then release the grip suddenly. Persistence of the grip or its slow relaxation in spite of the patient's efforts to release, suggests myotonia. Normal persons will be able to grip and relax quickly on command.

Percussion Myotonia

Tap sharply over the thenar eminence, brachioradialis, deltoid, quadriceps or calf muscles with a percussion hammer. If myotonia is present the depression produced by muscle contraction persists for several seconds. In the case of thenar eminence opposition of the thumb develops and it persists for several seconds before relaxing. Myotonia can be demonstrated in the tongue by percussing over the tongue, protruded over a wooden spatula kept under the tongue, to prevent injury from the teeth.

Myotonic reaction may be localized to certain group of muscles or it may be generalized. It is better elicited after a period of relaxation and it tends to reduce with repeated contractions of the affected muscles. Exposure to cold evokes or enhances myotonia.

Hereditary conditions showing myotonia are myotonia congenita, dystrophia myotonica, hyperkalemic periodic paralysis, paramyotonia and chondrodystrophic myotonia. Myotonia occurs in acquired disorders such as myxoedema and vitamin E deficiency. Certain drugs such as clofibrate may give rise to myotonia.

Abnormal Movements

A variety of characteristic abnormal movements (or hyperkinesias) resulting from involuntary contractions of voluntary muscles occur in several neurological disorders.

Hyperkinesias may affect any part of the body. They may result either from organic neurological lesions or they may be psychogenic. Metabolic abnormalities such as hepatic failure, respiratory failure, and uraemia and side effects caused by certain drugs (phenothiazines, reserpine, salbutamol and others) also lead to abnormal movements in the absence of primary neurological disease.

The following points should be noted when abnormal movements are present:

1. The part involved.
2. Rate, range, rhythm, speed and amplitude of the movements.
3. Whether they are present at rest, on adopting particular postures, or during voluntary activity.
4. The influence of fatigue, emotional tension, attention by others and sleep on these movements.
5. Whether the movements are stereotyped or constantly changing in pattern.

Those abnormal movements which fit into a specific clinical description include tremors, chorea, athetosis, myoclonus, hemiballism, dystonia, spasms, convulsions, tics, cramps and fasciculations.

If the pattern does not fit into the classic types it is better to describe the movement clearly, for clinical purposes.

Tremors

Tremors consist of a series of involuntary, rhythmic, regular and rapid oscillatory movements that result from the alternate contraction and relaxation of opposing groups of muscles. It is called 'simple tremor' when only one muscle group and its antagonist produce the involuntary movement. 'Compound tremors' result from contraction of several groups of muscles and their antagonists, producing a series of complex movements. Tremors may affect whole body or only a part. The rate of the oscillatory movement may be 3 to 5/ second (slow tremors), 5 to 10/ second (medium tremors) or 10 to 20/ second (rapid tremors). Their range may be fine, medium or coarse. The tremors may be present at rest (rest tremors) or they may appear or become more marked during voluntary activity (motor or intention tremors) or they may be present in a particular posture only (postural tremors). Emotional tension and attention tend to exacerbate organic tremors.

These organic tremors should be differentiated from physiologic tremors which appear at a frequency of 8 to12 oscillations per second during slow voluntary muscle contraction. They become more marked during tension, anxiety and fatigue.

Fine rapid tremors occur in thyrotoxicosis, drug intoxication, general paresis, anxiety state and in psychoneuroses. They are more easily demonstrable on the outstretched hands.

Coarse tremors are slow and are usually seen in parkinsonism, Wilson's disease, alcoholism and diseases of midbrain and cerebellum. Familial tremors may also be coarse and slow. Rest tremors (static tremors) are slow (2–6 sec), coarse, and compound type of tremors that disappear during voluntary activity and exacerbate during excitement and anxiety. The pill-rolling tremors of Parkinsonism are static tremors in which the thumb moves repeatedly on the first two fingers along with flexion extension movement of the wrist. The tremor comes down with voluntary activity.

'Intention tremors' or motor tremors are those which are absent at rest, but appear during voluntary activity. These tremors may be of medium amplitude and regular or they may be coarse, irregular and jerky. They can be demonstrated by making the patient touch the tip of his nose with his finger (finger-nose test). Tremors which occur only at the end of voluntary action are called 'terminal tremors'. This type of tremors are characteristically seen in cerebellar lesions.

Postural tremors are fine and more rapid than resting tremors, occurring at the rate of 8 to11/ sec. They can be brought out better by maintaining the limb in a particular posture, e.g. keeping the upper limbs and hands outstretched. They usually disappear during voluntary movements and at rest.

Familial tremor occurs in family members. This worsens during voluntary activity but disappears at rest. Benign tremors (essential tremors) are similar to familial tremors, but occur sporadically without a family history.

Psychogenic tremors are encountered in persons with anxiety neuroses. These tremors are usually of medium amplitude but may be fine or coarse. Although they may be present at rest, they are usually worsened by voluntary movements, tension, emotional stress, fatigue and anxiety.

Chorea

It is characterized by involuntary, purposeless, irregular arrhythmic and asymmetric movements, variable in type and location, constantly changing in form and affecting different parts of the body at irregular intervals. These movements may be present at rest, but are usually brought on or worsened by motor activity. They may affect any part of the body. In the face, they may appear as grimacing movements. When the upper limbs are held above the head, the limbs assume a position of hyperextension of the proximal and terminal phalanges, flexion and pronation of the wrist with arching of the hand (choreic hand). The other features of chorea include hypotonia of the limbs and pendular or hung-up deep tendon reflexes.

Chorea, occurring as a rheumatic manifestation, is called Sydenham's Chorea. It is particularly prone to aggravate during pregnancy (chorea gravidarum). Chorea may occur in Huntington's disease, metabolic encephalopathies and encephalitides. Senile Chorea occurs in older age groups.

Athetosis

These are involuntary, irregular, semirhythmic, writhing movements which are slower in rate, larger in range and more sustained than choreic movements, usually involving the distal parts of the extremities. Characteristically these movements result in a combination of flexion, extension, abduction, adduction, pronation and supination in varying degrees. These movements become exaggerated during voluntary activity and are associated with increased tone of the limbs. These movements may be congenital in origin or caused by acquired disorders of the caudate nucleus and putamen.

Involuntary movements which share the characteristics of chorea and athetosis are called choreoathetoid movements. Athetosis and similar abnormal movements are included under the term dystonias.

Myoclonus

It is an involuntary, abrupt, brief and rapid, jerky movement of a part of a muscle, entire muscle or a group of muscles. These movements are nonrhythmic, may be single, and random or repetitive. They may affect a part of the body or the whole body. They may occur at rest or during motor activity but are generally decreased during voluntary movement. They are seen in acute, subacute and chronic encephalitides, toxic, metabolic and hypoxic encephalopathies, and degenerative diseases of the brain. They may also occur rarely in diseases of spinal cord, spinal roots, and peripheral nerves. These movements may also be a part of seizure disorders. Myoclonic jerks unassociated with other neurological abnormalities occurring during sleep, particularly in children may be seen in the absence of organic disease.

Hemiballism

These are unilateral, purposeless, involuntary movements of larger amplitude, greater force and higher rate than choreic movements. Predominantly they affect the proximal portions of the limbs. The face and trunk muscles are generally spared. Hemiballism is caused by vascular lesions of the contralateral subthalamic nucleus or its connections.

Dystonias

Dystonia is an abnormal involuntary movement characterized by sustained muscle contractions, frequently causing twisting and repetitive movements or abnormal postures. Dystonic movements are usually slow, but quick components may also coexist causing confusion with myclonic jerks. They are arrhythmic and tend to aggravate with stress, fatigue and emotional upset but are relieved by sleep and rest. An interesting feature of dystonia is the patient's ability to suppress the movement by a sensory trick that is usually tactile or proprioceptive. According to the site of involvement dystonia may be classified as

i. Focal,
ii. Segmental,
iii. Multifocal,
iv. Hemidystonia or generalized.

Spasms

These are involuntary contractions of a single muscle or group of muscles. Spasms can be of two types-clonic and tonic. Clonic spasms are rapid, brief, repetitive contractions often resulting in movements of the affected part. Tonic spasms are prolonged or sustained contractions often resulting in either alteration of posture or limitation of movement. A painful, tonic spasm of a muscle is called 'cramp'. Spasms usually result from irritation of nerve fibers. Local painful conditions may lead to tonic or clonic muscle spasm with reflex rigidity. Mechanical stimulation of muscle may also produce a focal spasm. Tetanus and tetany produce characteristic muscle spasms due to hyperirritability of the nerves and muscles. Facial spasms are brief, repeated, clonic contractions of any of the muscles supplied by the facial nerve. Spasm affecting the orbicularis oculi muscle selectively is called 'blepharospasm'.

Tics (Syn: Habit Spasm)

Unlike spasms, tics are of psychogenic origin. A tic is a well co-ordinated, semipurposive, repetitive act, involving a group of muscles. Although tics start initially due to physical or emotional stress, later on they become stereotyped, brief, repetitive, involuntary movements occurring at irregular intervals. These movements can be suppressed to a certain

extent by voluntary effort, but they are usually compulsive in nature and aggravated by emotional stress.

Convulsions

These are violent, shaking, rhythmic movements caused by spasmodic alternating contraction of agonist and antagonist groups of muscles, often caused by irritative lesions in the brain. They are characteristically seen in generalized tonic-clonic epilepsy with the sequence of tonic, clonic and postictal stages. Convulsions may affect either a part of the body (partial) or the whole of it (generalized). Convulsions can also be seen in metabolic conditions such as hypoglycemia, hypocalcemia, uraemia and others.

Fasciculations

These are fine, flickering, irregular, inconsistent, single, rapid, twitchig movements due to involuntary contraction of a fasiculus of muscle fibers, when the muscle is at rest. They result from irritation of the lower motor neuron. Usually, they are visible as faint contractions under the skin surface, but are not strong enough to cause movement across joints. However, when they are coarse and affect the muscles of the hand, they may produce irregular involuntary movements of the fingers. So also prominent fasciculations of the tongue may give rise to movement. Fasciculations can be brought out or intensified by tapping the muscle, exposing it to cold, or by administering cholinergic drugs like prostigmine. Spinal anesthesia, peripheral nerve block and drugs like quinidine may abolish these movements. Although fasciculations may be seen due to any lesion that affects the lower motor unit, they are most frequently seen in degenerative diseases such as motor neuron disease, spinal muscular atrophy, progressive bulbar palsy and syringomyelia. Systemic disorders like uraemia, electrolyte disturbances and exposure to heavy metals may also produce widespread fasciculations.

Muscle Power

Muscle power is the force or strength of contraction that can be generated voluntarily by a muscle or agonist muscle groups. In normal individuals the power in different groups of muscles varies, according to their physiological requirements. In general, the larger the muscle, the greater the muscle power. However, there are exceptions to this statement. For instance, the power generated by the muscles of mastication in closing the jaws is considerably greater than the power generated by some of the larger muscles like pectoral muscles. In disease states such as muscular dystrophies, pseudohypertrophied muscles are weak in spite of their larger size. In disuse atrophy following prolonged immobilization of a limb, though the muscle size is reduced, power is relatively preserved to a greater degree.

There are two alternate methods to test the power of muscles.

i. Patient initiates the contraction and continues to do so against resistance offered by the examiner.
ii. Muscle to be tested is made to contract fully and the patient maintains this position, while the examiner tries to overcome it, e.g. The patient is asked to hold his upper limb in full extension at the elbow and the examiner tries to flex it.

The second method is better to bring out minimal grades of weakness.

Grading

The power of the muscles is objectively expressed in grades. This expresses the power in a semi quantitative manner. Medical Research Council (MRC) grading is generally adopted.

Grade 0	Complete paralysis with not even a flicker of movement
Grade 1	A flicker of movement is possible
Grade 2	The part can be moved, if gravity is eliminated by suitable positioning
Grade 3	The muscle can contract against gravity but not against any resistance.
Grade 4	Muscle can contract against mild or moderate resistance applied by the examiner.
Grade 5	Normal power is present. Movement against full resistance is possible.

Grading of power is useful to express variation in strength during the evolution and resolution of disease processes.

Principles to be Observed while Testing Power

Patient should be cooperative and should understand the command so as to generate maximum power. The movements should be smooth and not jerky. Proper positioning of the part is necessary to generate maximum power of contraction. The examiner should apply resistance gently and in a progressive manner. The muscle being tested should be inspected and palpated for contraction.

When the power is markedly reduced, proper positioning to eliminate the effect of gravity is necessary to bring out the movement. In normal persons muscle power varies with age, sex, body build and occupation. The examiner has to take these factors into consideration while assessing muscle power.

In comatose patients, normal infants and uncooperative children, classical method of testing is not possible. In them the following points should be observed to assess muscle power.

- Does he move the limbs voluntarily or spontaneously?
- Does he withdraw a limb purposefully to painful stimulus. If he does so, is the movement vigorous or weak?
- Are the spontaneous or withdrawal movements symmetrical or asymmetrical on both sides?
- In a comatose patient, when the limb is lifted from the bed and dropped, does it just drop down or is there any resistance?

Before attributing weakness of muscles to neurological causes, several non-neurological conditions which reduce strength of contraction have to be excluded. These include painful conditions, deformities of joints, involuntary movements and extreme degrees of spasticity and rigidity. (Figs 1 to 28).

Hysterical Paralysis

Some hysterical patients may mimic muscle paralysis. This has to be distinguished from genuine paralysis.

1. The hysterical patient responds with the opposite movement when instructed to perform any movement.
2. The contractions are irregular, jerky and poorly sustained.
3. He may produce a brief good contraction but suddenly relaxes the muscle resulting in a 'giving way' response.
4. Lack of the 'follow through' response. In normal persons while testing muscle power, if the examiner suddenly releases the resistance, the limb continues to move in the same direction before it stops. In hysterical subjects this does not happen.

Muscle Power in Different Neurological Disorders

UMN lesions result in paralysis of voluntary movements whereas LMN produces paralysis of individual muscles or muscle groups. In suspected UMN lesions it is sufficient to examine the motor power of various movements in a rapid survey, but it is very necessary to examine individual muscles if LMN lesion is suspected. Although cerebellar lesions do not impair muscle power per se, they interfere with voluntary movement considerably. Since full testing of individual muscles is time consuming, taxing to both patient and the examiner, and often unnecessary, a rapid assessment of muscle power can be made by a "mini muscle power testing".

Mini Muscle Power Testing

We suggest this as a short, quick, systematic method to assess muscle power, suitable for routine survey.

Movements to be Tested

Upper Extremities

Hand grip, flexion and extension at wrists, flexion and extension at elbow, pronation and supination of the forearm, abduction, adduction, flexion and extension at the shoulders.

Lower Extremities

Extension and flexion of big toe and other toes, dorsiflexion, plantar flexion, eversion and inversion of foot, flexion and extension of knee, flexion, extension, adduction, and abduction at the hip.

Trunk

Lifting up the head from the bed and raising the lower limbs straight from the bed give rise to active

contraction of abdominal muscles which can be seen to contract and can be palpated. If the upper or lower abdominal muscles are paralysed the umbilicus is pulled by the actively contracting muscles towards their side. This is called 'Beever's sign'. A rapid assessment of the power of the proximal muscles of the lower limb can be made by asking the patient to get up from the sitting position and walk.

Detailed Muscle Power Testing

Power of individual muscles should be tested under the following situations:

a. If there is restricted weakness in one group of muscles in a limb on mini muscle power testing.
b. If there is differential weakness of muscles, i.e. some muscles are more affected than the others and some others are completely spared, and
c. If the history and physical examination suggests a lower motor neuron type of paralysis.

Testing Muscle Power in Myasthenia

Clinically myasthenia manifests as easy fatigability of the voluntary muscles when put to repeated contractions. Conventional testing of muscle power may not reveal any abnormality and mild cases may be missed.

Test

i. Ask the patient to look up continuously for sometime and observe whether he develops ptosis.
ii. Alternatively ask him to move his eyes rhythmically in both the horizontal and vertical directions and then observe the range of movements in all directions. Look for paresis of ocular movements which clears up after a period of rest.
iii. Ask him to hold his upper limbs abducted at the level of the shoulders for 30 seconds and observe for weakness of shoulder muscles.
iv. Ask him to walk up and down a flight of stairs or to do sit-ups several times, observe for weakness of the pelvic girdle muscles.

Descriptive Terms Used for Different Patterns of Paralysis

1. *Hemiplegia:* Paralysis of upper and lower limbs on the same side of the body with or without involvement of the face. This is due to UMN lesion.
2. *Monoplegia:* Paralysis of all muscles in one limb, either upper (brachial monoplegia) or lower limb (crural monoplegia).
3. *Bilateral hemiplegia (Syn: tetraplegia):* Paralysis of upper and lower limbs on both sides with poor head and trunk control.
4. *Quadriplegia:* Paralysis of all four limbs and the trunk due to upper or lower motor neuron lesions.
5. *Paraplegia:* Paralysis of both lower limbs due to upper or lower motor neuron lesions.

 Diplegia is a special form of congenital paraplegia in which the lower limbs are very spastic and considerably more affected than the upper limbs. This is caused by bilateral cortical lesion.
6. *Paraplegia in flexion:* The paralysed lower limbs are kept in a state of flexion at the hips and knees with the feet and toes dorsiflexed. This posture occurs in the chronic stage of a severe or total spinal cord damage, usually in the high cervical cord region. Sometimes, it also occurs in advanced degenerative disease of the brain—cerebral paraplegia in flexion.
7. *Paraplegia in extension:* The paralyzed lower limbs are kept in a state of extension at the hips and knees with adduction of the thighs. This posture develops in the chronic stage of partial or incomplete spinal cord damage at lower levels.
8. *Mononeuritis:* Motor-sensory paralysis in the distribution of one peripheral nerve.
9. *Mononeuritis multiplex:* Motor-sensory paralysis in the distribution of multiple peripheral nerves, occurring asymmetrically.
10. *Polyneuritis:* Motor-sensory paralysis in the distribution of multiple peripheral nerves occurring symmetrically.

Examination of Reflexes

Definition

A reflex is consistent involuntary adaptive response to the stimulation of a sense organ.

Components

Normal reflex depends upon the integrity of the reflex arc which consists of:

i. Sensory receptor
ii. Afferent pathway to convey the impulse from the receptor to the center.
iii. Reflex center in the central nervous system-spinal cord or brainstem.
iv. Efferent pathway from the reflex center to the periphery, and
v. Effector organ which responds to the sensory stimulus.

This response may be motor, visceral or secretory.

Types of Reflexes

Reflexes can be grouped into four categories for purposes of neurological examination.

1. Deep reflexes (muscle stretch reflexes)
2. Superficial reflexes
3. Visceral or organic reflexes
4. Miscellaneous reflexes

1. *Deep reflexes:* These are the reflexes elicited by a sudden stretch of a muscle and hence they are better termed 'muscle stretch reflexes' (MSR). The terms such as tendon reflexes, deep tendon reflexes, periosteal reflexes and myotactic reflexes are also used synonymously. All these are monosynaptic reflexes, e.g. biceps, triceps, knee and ankle reflexes.
2. *Superficial reflexes:* These are the reflexes elicited by stimulating the skin or mucous membrane. These are polysynaptic reflexes, e.g. abdominal and corneal reflexes.
3. *Visceral or organic reflexes:* These are the reflexes which result in contraction of the viscera, e.g. micturition, defecation and deglutition reflexes.
4. *Miscellaneous reflexes:* Postural reflexes, conditioned reflexes, cerebral reflexes, autonomic reflexes and others.

Since most of these reflexes have no application in clinical neurology such of these will not be discussed further.

Importance of Examination of Reflexes

Most of the reflexes may appear to have no definite function in health, but certainly they are more informative in clinical neurology. To elicit MSR properly, the muscles should be relaxed, and optimally stretched, and the stimulus should be adequate. Examination of the reflexes is of special importance because of the following reasons. Many reflexes are not dependent on the attention, level of consciousness, intelligence or cooperation of the patient as in the cases of sensory or motor examination. They provide objective evidence of organic neurological disease. Sometimes they may reveal earliest evidence of subtle disturbances in the nervous system. They give clues to the integrity of the sensory and motor pathways and the reflex arc. Since the centers for the various reflexes are located in particular regions of the central nervous system they help to localize the lesion. Hence, knowledge of the neuroanatomy of various reflex arcs is essential for their proper interpretation (Table 32.16).

Table 32.16: Neuroanatomy of the commonly elicited reflexes

Reflex	*Afferent pathway*	*Center*	*Efferent pathway*
1. *Muscle stretch reflexes*			
• Jaw jerk (masseter and temporalis muscles)	Cranial nerve V	Pons	Cranial nerve V
• Bicep reflex (biceps muscle)	Musculocutaneous n	C5-6	Musculocutaneous
• Triceps reflex (triceps muscle)	Radial n	C6-7	Radial n
• Supinator reflex (brachioradialis muscle, Syn: supinator longus)	Radial n	C5-6	Radial n

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Reflex	*Afferent pathway*	*Center*	*Efferent pathway*
• Knee reflex (quadriceps femoris, mainly vastus medialis muscle)	Femoral n	L2,3,4	Femoral n
• Ankle reflex (calf muscles gastrocnemius, soleus, plantaris)	Tibial n	L5, S1-2	Tibial n
2. *Superficial reflexes*			
• Corneal reflex	Cranial nerve V	Pons	Cranial nerve VII
• Conjunctival reflex	Cranial nerve V	Pons	Cranial nerve VII
• Pharyngeal reflex	Cranial nerve IX	Medulla	Cranial nerve X
• Palatal reflex	Cranial nerve IX	Medulla	Cranial nerve X
• *Abdominal reflexes:*			
- Upper	T6-9 posterior roots	T6-9 cord segments	T6-9 anterior roots
- Middle	T9-11 posterior roots	T9-11 cord segments	T9-11 anterior roots
- Lower	T11-Ll posterior roots	T11-Ll cord segments	T11-L1 anterior
• Cremasteric reflex	Femoral n	Ll,2	Genitofemoral n
• Plantar reflex	Tibial n	L5,Sl,2	Tibial n
• Anal reflex	Pudendal n	S3,4,5	Pudendal n
• Bulbocavernosus reflex	Pudendal n	S3,4	Pudendal n

Testing Muscle Stretch Reflexes (Table 32.17)

Note: In the following description (Table 32.17), all the reflexes are elicited with the patient in supine position in bed. Depending on the convenience of the patient and the examiner, other postures can be adopted.

Reinforcement of Muscle Stretch Reflexes

When a reflex is difficult to elicit in spite of good relaxation of the muscles concerned, and employing correct technique of elicitation, effort should be made to reinforce the reflex, before concluding that it is absent. By reinforcement the threshold for muscle contraction is diminished and the contraction is elicited better.

For reinforcing the reflexes in the lower limbs the patient is instructed either to hook the fingers of one hand to those of the other and then strongly pull them apart (Fig. 32.36) or to make a fist forcefully, while eliciting the reflexes. To reinforce the reflexes in the upper limbs, the patient is asked to clench his jaws tightly or to press the sale of the foot strongly against the foot board of his bed.

Sometimes, reflexes may become elicitable only after applying reinforcement techniques and such reflexes can be taken as normal. Even after reinforcement if a reflex cannot be elicited, it has pathological significance.

Clonus

This term denotes a series of rhythmic, involuntary muscle contractions, induced by sudden passive stretch of a tendon. At times, it may occur spontaneously too. A true clonus persists as long as the stretch on the muscle is maintained. This occurs in extensive UMN lesions, and is always associated with exaggerated muscle stretch reflexes and spasticity. Instead of sustained clonus a few ill sustained clonic movements may be present at the start of the muscle stretch which soon fade out even when the stretch is maintained. Such clonic movements are irregular in rate and rhythm. This is called pseudoclonus. Several non-neurological conditions that are associated with brisk muscle stretch reflexes, do not produce true clonus.

Table 32.17: Method to elicit muscle stretch reflexes (Figs 32.33 to 32.38)

Reflex	*Method*	*Normal responses*	*Abnormality and remarks*
1. Jaw reflex	Ask the patient to open his mouth partially. Keep your left index finger horizontally on the patient's chin gently pressing it downwards. Strike on your finger with the knee hammer bringing it from above downwards. Watch the movement of the lower jaw	No contraction or mild contraction not strong enough to produce any appreciable movement of the jaw	Absence of jaw reflex may not be significant since it may occur in normal persons. Exaggerated response occurs in bilateral UMN lesion of fifth cranial nerve. Unilateral UMN lesion does not affect this reflex grossly
2. Biceps reflex	Keep the elbow flexed to 30-40º and resting on the bed while forearm and hand rest relaxed on the abdomen. Place your left index and middle fingers on the biceps tendon with sufficient pressure to stretch the biceps tendon. Strike on your fingers with the hammer (Fig. 32.33A)	Contraction of biceps-flexion of forearm at the elbow—to some degree, supination of forearm	Absent response—no contraction of biceps, no flexion or supination of the forearm. LMN lesions at C5,6 spinal segments or roots. Exaggerated response—exaggerated flexion and supination of the forearm along with flexion at the wrist and fingers and adduction of the thumb. UMN lesion above C5 spinal segment
3. Supinator reflex (Syn: brachioradialis reflex, radial periosteal reflex)	Keep the upper limbs in the same position as for biceps reflex except that the forearms should be kept in midpronation. Strike directly on the distal portion of radius just proximal to the styloid process. Observe the movement and palpate the brachioradialis muscle (Fig. 32.33B)	Contraction of brachioradialis-flexion of the forearm at the elbow and supination of the forearm may occur	Absent response—no contraction of brachioradialis, no flexion or supination of the forearm—LMN lesion at C5,6 spinal segments or roots. Exaggerated response—exaggerated flexion or supination of the forearm, along with flexion at the wrist and fingers and adduction of the thumb. UMN lesions above C5 spinal segment. Inverted response—no flexion or supination of the forearm. Only marked flexion at the wrist and fingers due to a lesion at C5 spinal segment involving the pyramidal tracts as well
4. Triceps reflex	Keep the upper limbs in the same position as for biceps reflex. With your left hand hold the patient's wrist and pull the forearm slightly towards midline so that the elbow is lifted slightly above the bed. Strike the triceps tendon with the hammer and watch for contraction of triceps and extension at the elbow (Fig. 32.33C)	Contraction of the triceps muscle—extension of the forearm at the elbow	Absent response—no contraction of triceps, no extension of the forearm. LMN lesion at C6,7 spinal segments or roots Exaggerated response—exaggerated extension of the forearm, UMN lesion above C6 spinal segment. Paradoxical flexion response—instead of of extension, flexion of the forearm takes place due to unopposed action of normal biceps muscle. Lesion at C6,7 spinal segments
5. Finger flexion reflex C8-T1 spinal segments and roots. Median and ulnar nerves. Flexor digitorum profundus muscle	Hold the patient's hand with your left hand so that his palm faces up and your palm faces down producing slight extension at the patient's wrist and flexion at the metacarpophalangeal and interphalangeal joints. Ask him to rest the weight of his forearm and hand on your hand. Tap lightly the dorsum of your fingers with the hammer. Observe and feel the movements of his fingers	Gentle flexion of fingers or no response on both sides	The reflex may be exaggerated or asymmetrical between the sides. This reflex does not give any additional help in neurological localization, but exaggeration or asymmetry should suggest UMN lesion on the abnormal side above C5
6. Hoffman's reflex C8- T1 spinal segments and roots, median. Flexor digitorum profundus muscle	Hold the sides of middle phalanx of the middle finger of the patient between your left thumb and index finger. Hold terminal phalanx of the same finger with your right thumb and index finger and suddenly and forcefully flex it at the terminal interphalangeal joint. Immediately release the terminal phalanx so that it pops up into extension. Watch the movements of other fingers and thumb (Fig. 32.34)	No visible movements of the other fingers or thumb	Exaggerated flexion of fingers and thumb or asymmetrical response on both sides occurs in UMN lesion, above C8. This has no additional localizing value

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Reflex	*Method*	*Normal responses*	*Abnormality and remarks*
7. Knee reflex (Syn: Quadriceps femoris reflex)	Keep the hip and knee slightly flexed to 30-45º and support the limb at knee with your left forearm or hand and ask the patient to relax the limb muscles by allowing his limb to rest completely on your hand. Strike the patellar tendon with hammer, watch for quadriceps contraction and movement of the leg (Fig. 32.35A)	Contraction of the quadriceps muscle extension of the leg at the knee *Note:* This was the first MSR to be introduced into clinical neurology. Hence, the percussion hammer came to be known as 'knee' hammer	Absent response—no contraction of the quadriceps, no extension of the leg. LMN lesion at L2,3,4 spinal segments or roots Brisk response—extension of the leg is abrupt and amplitude of movement is larger. Exaggerated response—in addition to the extension of the leg. There will be adduction of the thigh on the same side and occasionally on the opposite side also. Sometimes, extension of the leg on the opposite side may also occur The best position to elicit knee reflex is with the leg hanging down freely from the edge of the bed. Pendular knee jerk occurs in cerebellar diseases. This phenomenon can be demonstrated only with the leg hanging down (see page 464)
8. Ankle reflex (Syn: Achilles reflex)	Keep the lower limb slightly flexed and externally rotated at hip, slightly flexed at the knee and the ankle resting on the other leg. Slightly dorsiflex the foot to stretch the tendon and strike with the hammer on the tendon. Observe contraction of the calf muscles and movement at the ankle (Fig. 32.35B)	Contraction of calf muscles, i.e. gastrocnemius, soleus	Absent response—no contraction of calf muscles, no plantar flexion of the foot. LMN lesion at (L5), segments or roots. *Note:* In many healthy elderly individuals ankle jerks may be absent. Exaggerated response—exaggerated plantar flexion of the foot. Sometimes, tapping on the sole of the foot (medial plantar response) or on dorsum of the ankle (paradoxical response) produces plantar flexion of the foot due to UMN lesion above L5 spinal segment In hypothyroidism the ankle jerks show delayed relaxation. This is best demonstrable if the patient kneels on the bed with the feet projecting out, and the tap is given with the foot slightly dorsiflexed



Figs 32.33A to C: Testing the reflex in the upper limb. (*See* text for details). The arrows show the direction of jerk of the forearm (A) Biceps reflex, (B) Supinator reflex, (C) Triceps reflex



Fig. 32.34: Hoffman's reflex. (*See* text for details)

Grading of Muscle Stretch Reflex (MSR) (Table 32.18)

The following parameters are considered:

i. Rapidity and the speed with which the muscle contraction occurs after giving the stretch stimulus.This is the most important parameter. Palpation of the contracting muscles helps to assess the speed of its contraction.
ii. The amplitude or range of the movement, and
iii. The rapidity with which the movement is arrested, i.e. duration of the response.





Figs 32.35A and B: (A) Eliciting knee reflex; (B) Eliciting ankle reflex (*See* text for details)



Fig. 32.36: Eliciting knee reflex with reinforcement. Note the tight grip made by the patient while doing the test (*See* text for details)



Fig. 32.37: Testing ankle clonus (*See* text)



Fig. 32.38: Eliciting patellar clonus (*See* text for details)

Table 32.18: Characteristics of muscle stretch reflexes of various grades

Parameter	*Diminished*	*Brisk*	*Exaggerated*	*Hyperactive*
Speed (latent period)	Variable	Increased	Increased	Decreased
Range of movement	Decreased	Normal	Increased	Increased
Duration of contraction	Decreased	Normal	Increased	Increased

Based on these observations a reflex is subjectively graded and expressed according to any of the three grading systems given below:

1	*2*	*3*	*Remark*
Absent	0	0	No contraction is elicited even on reinforcement
Diminished (sluggish)	1	+	Slow and mild contraction, sometimes requiring repeated stimuli
Normal	2	++	Normal contraction and quick relaxation
Brisk	3	+++	Increased speed with normal range of movement and duration of contraction
Exaggerated	4	++++	Increased speed and amplitude and sustained contraction
Associated with clonus	5	+++++	In addition to the above, clonus is elicitable

The term hyperactive reflex is used to denote increased amplitude and duration, but reduced speed of contraction.

Quantitative Changes in Muscle Stretch Reflexes

MSR may be absent or diminished physiologically or pathologically. Symmetrical loss of reflexes may occur in 3 to 10 % of normal people and loss of ankle reflexes alone may occur in many healthy elderly individuals. Asymmetrical loss of reflexes is always pathological, suggestive of LMN lesion. Muscle stretch reflexs (MSR) may be brisk in some normal persons especially when they are anxious, nervous or tense, but they are bilaterally symmetrical and are not associated with muscle weakness, spasticity, extensor plantar response or true clonus. Asymmetrical brisk MSR are always pathological and suggestive of UMN lesion.

Bilateral, symmetrical brisk or exaggerated MSR are pathological if they are associated with muscle weakness, spasticity, extensor plantar responses and/or true clonus.

Note: Although clinically, hyperreflexia in UMN lesions is accepted as due to damage to the pyramidal tracts, pathophysiologically, it is the result of damage to the reticulospinal and vestibulospinal tracts which descend along with the pyramidal tracts.

Qualitative Changes in Muscle Stretch Reflexes

1. *Inversion of MSR:* This is an abnormal phenomenon in which, when a MSR is elicited, instead of the expected muscle group contracting, another group of muscles contracts, e.g. inversion of supinator reflex. This phenomenon occurs due to a combination of LMN lesion and also UMN lesion at C5 spinal segment level. It has a very definite localizing value.
2. *Paradoxical MSR:* This is an abnormal phenomenon in which, when a MSR is elicited, instead of the normal expected movements the opposite movement takes place, e.g. paradoxical triceps jerk. This phenomenon occurs sometimes when there is a LMN lesion in the reflex center. The normal, antagonist muscles contract unopposed giving rise to the paradoxical movement.
3. *Spuriously brisk MSR:* An MSR may appear brisk when the antagonist muscles are weak, due to a LMN lesion. For example, in the presence of LMN lesion of the hamstring muscles, the knee reflex may appear to be brisk.

Methods to Elicit Clonus

Ankle clonus: The patient lies supine in bed. Both the hip and knee are fixed to 90°. Support the calf on your left palm and with the right hand holding the foot, suddenly stretch the tendo-Achilles by a sharp dorsiflexion. Slight eversion of the foot helps to elicit the reflex more readily. The foot goes into clonic movements (Fig. 32.37).

Patellar clonus: Keeping the lower limb straight and relaxed, the patella is grasped between the index finger and the thumb and suddenly pushed down to stretch the quadriceps tendon. The patella goes

into clonus, as long as the stretch on the tendon is maintained (Fig. 32.38).

Wrist clonus: This can be elicited by suddenly hyperextending the wrist and maintaining the stretch on the long flexors of the hand.

SUPERFICIAL REFLEXES

Abdominal Reflexes (T6–L1 Spinal Segments and Roots)

The abdominal reflexes are elicited by stroking the skin of the abdominal wall (Fig. 32.39). Upper abdominal (T6– T9 spinal segments), midabdominal (T9–T11 spinal segments) and lower abdominal (T11–L1 spinal segments) should be tested individually on both sides. To elicit these reflexes the patient should lie supine with the abdominal muscles kept relaxed. Using a blunt object like the handle of a reflex hammer or a key, the skin of the abdominal wall is stroked horizontally from lateral side towards the midline, above, at, and below the level of the umbilicus on both sides, during the end of expiration. A normal response is a brief and brisk contraction of the abdominal musculature, which results in visible movement of the umbilicus towards the side of stimulation.

In obese individuals, multiparous women and when the abdomen is distended or is kept rigid, abdominal reflexes may be absent even in health. These reflexes are pathologically lost when there is upper motor neuron lesion, i.e. pyramidal tract lesion above the level of the reflex arc or in lower motor neuron lesions affecting the corresponding reflex arc. Sometimes in obese individuals and those with lax abdominal walls the movement of the umbilicus may not be visible. Still the contraction of abdominal muscles can be palpated.

Cremasteric Reflex

(L1-2 Spinal Segments and Roots)

With the patient in supine position and the lower limbs slightly abducted, the skin on the upper and inner aspect of the thigh is stroked with the same object used for eliciting the abdominal reflexes (Fig. 32.40). The normal response is a reflex contraction of the cremasteric muscle resulting in visible elevation of the testicle on the stimulated side. Like the abdominal reflex, this reflex is lost in upper motor neuron lesions above the level of L2 spinal segment or lower motor neuron lesion involving the reflex arc.

Explanation for absence of abdominal and cremasteric reflexes in pyramidal tract lesions: These reflexes have a cortical pathway in addition to a spinal reflex arc. The afferent path travels up in spinal cord up to the parietal cortex and the efferent fibers descend to the anterior horn cells in the spinal cord through or in close association with pyramidal tract. A lesion in the pyramidal tract, anywhere in its course also involves these cortical loop fibers. This leads to abolition of these reflexes.

Other qualitative changes in the superifical reflexes include brisk reflexes and easy fatigability. Brisk reflexes may occur in the following conditions:



Fig. 32.39: Eliciting abdominal reflex. (*See* text for details)



Fig. 32.40: Eliciting cremasteric reflex. Method stroke the area shown. Look directly for contraction of the ipsilateral scrotum. (*See* text for details)

1. Anxious and psychoneurotic persons.
2. Parkinsonism and other extrapyramidal diseases in which a center in the midbrain which normally inhibits superficial reflexes may be involved.

Easy fatigability of these reflexes may be an early sign of UMN lesion. Asymmetrical loss of abdominal and cremasteric reflexes is always pathological, whereas symmetrical loss may sometimes occur physiologically or due to non-neurological causes.

Anal Reflex

(S3,4 Spinal Segments and Roots)

This reflex tests the contraction of the external anal sphincter in response to stimulation of the perianal skin.

One finger of the gloved hand of the examiner is inserted into the anal canal of the patient who lies in the lateral decubitus and the perianal skin is pricked or scratched with a pin. The reflex contraction of external anal sphincter can be felt, on the finger in the anal canal.

Bulbocavernosus Reflex (S3,4 Spinal Segments and Roots)

One hand of the examiner is placed over the perineum of the patient below the root of the penis while the foreskin or glans penis is pricked or pinched with the other hand. The reflex contraction of the bulbocavernosus muscle can be felt by the hand, placed over the perineum.

Plantar Reflex and (L5, S1,2 Spinal Segments and Roots)

There are several methods of eliciting plantar reflex. However, the method of Babinski is probably the most sensitive, and reliable method and hence, this is more widely adopted.

Babinski's Method

The patient lies supine with his lower limb in full extension. Employing the handle of a reflex hammer or a key or a small nail file, the lateral aspect of the plantar surface of the foot is stimulated beginning at the heel and moving up to the ball of the foot, but not up to the great toes. The movements of the great toe and other toes of the foot and leg in response to this stimulation are observed. In normal adults this stimulus results in a "flexor plantar response" characterized by initial flexion movement of the great toes and other toe (Figs 32.41A and B).

Response to stroking of the sole of the foot in normal subjects is given below:

a. Mild stimulus: Contraction of tensor fascia lata and contraction of adductors of the thigh.
b. Stronger stimulus: As in above + flexion of the outer four toes.
c. Still stronger stimulus: As in above + flexion of great toe, dorsiflexion of foot and inversion (flexor plantar response).
d. Maximal stimulus: Withdrawal of the limb.

If there is a slow and steady extension or dorsiflexion of the great toe followed by extension and fanning out of other toes in response to the





Figs 32.41A and B: Testing the plantar reflex. Babinski's method (A) Commencing to stroke the sole of the foot laterally, (B) Towards the end of the stroke. Note movements of the big toes and other toes (*See* text for description)

plantar stimulation, the response is called "classical extensor plantar response" or Babinski's sign. This is seen in upper motor neuron lesions above L_5 spinal segment. Occasionally the extension of great toe may be followed by flexion movement of the other toes, instead of fanning out, the lateral toes show no movement at all. This type of response is also called 'extensor plantar response', and it also indicates upper motor neuron lesion above L_5 spinal segment. The sequence of events taking place in extensor plantar response is extension of big toe, fanning and extension of lateral four toes, dorsiflexion of foot and flexion at knee and hip.

Fallacies

In UMN lesion, stroking the posterior and lateral border of foot produces extensor plantar response whereas stroking firmly the middle of the sole may produce flexion of the toes due to direct stimulation of short flexor muscles. An 'extensor plantar' response obtained when the lower limb is kept in full extension may tend to become a flexor response, if elicited with the leg kept flexed at the knee. Sometimes downward pressure on the distal part of the thigh so as to produce hyperextension at the knee may convert an equivocal plantar response into an extensor response.

An extensor plantar response indicates a lesion in the corticospinal tract. Sometimes in spite of adequate plantar stimulation, there may not be any movement in the great toe or other toes. This can occur in normal individuals with a very thick skin over the sole of the foot or in lesions of the afferent or efferent arc of this reflex. This is called a 'mute' or 'equivocal' response.

In anxious individuals or in patients with peripheral sensory neuropathy or when an unduly sharp stimulus is given, the patient quickly pulls the foot back away from the stimulus. This is called a "withdrawal response".

Other methods of eliciting plantar response: There are several methods to elicit plantar response, especially an extensor response. In UMN lesions the reflexogenic zone over the lower limb extends. Hence, these techniques employ stimulation of areas other than the sole of the foot. When the sole of the foot cannot be stimulated due to any reason these alternative methods become useful.

1. Chaddock's sign	Stimulate the lateral aspect of the foot, under and around the external malleolus in a circular direction.
2. Schäffer's sign	Apply deep pressure on the tendo-Achilles.
3. Gordon's sign	Squeeze the calf muscles.
4. Oppenheim's sign	Applying pressure, stroke with the thumb and index finger on the medial side of the shin of the tibia from the knee towards the ankle.

In all these methods the response is the same as described for classical extensor plantar response (Figs 32.42A to C).

It should be reiterated here again that Babinski's sign is the most sensitive, delicate, early and reliable sign of a corticospinal tract lesion. For the other signs of UMN lesion to be evident, it may be that the lesion in the corticospinal tract has to be an extensive one or more advanced. Just like reinforcement techniques in the case of muscle



Figs 32.42A to C: Alternate methods of eliciting plantar response
(A) Chaddock's sign, (B) Schäffer's sign, (C) Oppenheim's sign

stretch reflexes, simultaneous application of any two of the above methods, is occasionally of value of bring forth a latent extensor plantar response.

An extensor plantar response (Babinski's sign) may be obtained in the following conditions:

i. Lesion of the corticospinal tract constantly extensor on the affected side.
ii. Immediately after generalized convulsion bilateral and transient
iii. During sleep—bilateral and transient.
iv. In deep coma due to any etiology—bilateral and persistent
v. In normal infants-up to the age of 1 year bilaterally extensor.

Inversion of plantar reflex: In selective paralysis of short flexors of toes, plantar response may be "extensor" due to unopposed action of extensor group of muscles.

Tonic plantar reflex: While eliciting the plantar reflex, sometimes, the toes adduct and flex with persistent plantar flexion of the foot for a couple of minutes. This sign is indicative of lesion in the ipsilateral or contralateral prefrontal cortex and extrapyramidal system. This is one of the release reflexes.

Crossed Extensor Plantar Response

In severe spastic paraplegia, while eliciting plantar response on one side, in addition to extensor plantar response on the same side, there may be automatic extensor plantar response on the other side as well.

Primitive Reflexes (Syn: Release Reflexes)

Several types of reflex responses can be evoked in patients with advanced, diffuse diseases of the brain or with localized lesions in the frontal lobes. Some of these reflexes are present at birth or in early infancy and disappear as cortical control develops. Hence, these reflexes are referred to as 'primitive reflexes'. Later in life these reflexes may reappear due to diffuse cerebral damage because the subcortical nervous structures are released from the influence of higher cortical control. Hence, they are also referred to as "release reflexes". The student should look for these reflexes as their presence indicates diffuse cerebral disease.

i. *Grasp reflex:* When the palm is touched with the fingers of the examiner, especially on the radial border between the thumb and index finger, the patient's fingers involuntarily flex slowly and grasp the examiner's fingers. Sometimes the grasp may be so firm that the patient can be lifted off his bed. This is seen in contralateral frontal lobe lesions.
ii. *Groping reflex:* Mere sight of the examiner's fingers approaching the patient's hand results in the movement of his hand to grasp the examiner's fingers. This has the same significance as that of grasp reflex.
iii. *Avoiding reflex:* This is elicited by touching the skin on the ulnar border of the hand. The patient's hand reflexly moves away from the stimulus. It is present in patients with lesions in the contralateral parietal lobe or its connections.
iv. *Palmomental reflex:* This is elicited by stroking the skin on the thenar eminence of the hand, with a blunt object such as the handle of knee hammer. Puckering of the skin over the chin, caused by contraction of ipsilateral mentalis muscle will be observed, if this sign is present. (Fig. 32.43).
v. *Sucking reflex:* Light touch on the corner of the mouth results in involuntary opening of the mouth as though the patient is trying to suck something.
vi. *Snout reflex:* Light taps on the lips with the examiner's finger result in puckering and protrusion of the lips. *See* Figure 32.20 see also page 436.
vii. *Glabellar reflex:* This is elicited by tapping the glabella (root of the nose) repeatedly with the examiner's finger brought from above and behind the patient's head. In a normal individual, this results in blinking response to



Fig. 32.43: Eliciting Palmo-mental reflex. Stroke on the palm and watch for puckering movements over the chin on the same side (arrow)

the first 2 or 3 taps, but subsequent taps do not evoke any response. But in patients with parkinsonism and other diffuse degenerative diseases of the brain, the blinking continues as long as the taps are given. *See* Figure 32.19.

viii. *Mass reflex:* It is a reflex of spinal automatism. In severe spinal cord damage, sometimes, trivial sensory stimuli to any part of the body below the level of lesion such as weight of the bed sheets, light touch, movement of the foot or even elicitation of reflexes in the lower limbs, result in evacuation of the bladder and bowel, sweating, piloerection, penile erection and ejaculation, accompanied by slow, tonic flexion of the lower limbs at the hips, and knees. Sometimes, only the limb flexion component of the mass reflex may be present and this is called 'spinal defence flexion reflex'. This reflex should not be mistaken for return of motor power or improvement.

Examination of Sensory System

This part of the neurological examination is the most difficult one because perception of sensations is purely a subjective phenomenon, varying from person-to-person. Moreover the methods employed to test them also tend to be crude and subjective. The patient's responses depend largely on his level of consciousness, intelligence, attention, co-operation, and fatigue. Even in normal subjects the perception threshold and the appreciation of sensations differ in different areas of the body and in the same area under different conditions.

Aims of sensory examination are:

i. To detect the presence of absence of sensory abnormalities.
ii. To detect the pattern of sensory alterations which will help to localize the site of lesion in the sensory pathway, and
iii. To help in the follow-up of the illness.

While performing sensory examination the following general points should be borne in mind.

i. Sensory examination should be performed when the patient is not fatigued and he is still attentive and cooperative. In children and apprehensive adults, it is better to perform this part of the examination at the end of neurological examination since a detailed sensory examination often tires out the patient.
ii. The procedure and the expected response should be briefly and clearly explained to the patient by demonstrating on the normal side first under his direct vision. He should be instructed to give precise and brief answers.
iii. Once he has understood the procedure, perform the test, keeping his eyes closed so as to avoid distraction and any clue from direct vision.
iv. Start testing the sensations from the face and proceed downwards, always comparing the responses from the corresponding areas on either side.
v. Leading questions should be avoided.
vi. While mapping out the areas of sensory abnormality, proceed from the abnormal to normal area. This gives better definition of the border zone than proceeding from normal to abnormal area.
vii. In addition to his replies observe his emotional response also.

Once the sensory abnormality is detected, the next step is to localize the site of lesion in the sensory pathway.

Grading of Sensory Loss

There is no commonly accepted grading system to quantify sensory loss. Any such attempt tends to be arbitrary. However, the impairment of any sensation can be broadly quantified as mild, moderate, severe on total loss. Still a semiquantitative grading system may be applied as a guide to assess progress of the illness.

Mild sensory impairment	20–30%	diminution as compared to normal side
Moderate sensory impairment	30–70%	Do
Severe sensory impairment	more than 75%	Do

Sensory impairment of less than 15 % need not be always pathological. To grade a sensation, the patient is asked to quantify and express in his own words the appreciation of the sensation relative to the normal side and his response is recorded.

Method of Testing

Systematic detailed sensory examination all over the body is a tiring and time consuming procedure

which may not be necessary in all cases, especially those with no sensory symptoms. Such cases can be readily sorted out by a rapid minisensory survey. Those in whom this preliminary examination reveals abnormalities and those with sensory symptoms should have full detailed sensory testing.

Mini-sensory Examination

Examine touch and pin prick, over the face, proximal and distal parts of the limbs, and over chest and abdomen on both sides. Sense of position and passive movement are to be tested in both thumbs and great toes.

Detailed Sensory Examination

Primary modalities of sensation are touch, pain, temperature and vibration. The discriminative modalities are two point discrimination, stereognosis, graphesthesia, identification of difference in temperature and such others. Vibration is a composite sensation comprising touch and rapid alteration in deep pressure sense. Crude appreciation of the primary modalities occurs in the thalamus. Discriminative modalities are appreciated in the sensory cortex.

For the purpose of clinical testing, sensations can be classified as:

1. Superficial sensations: Sense of touch, pain and temperature.
2. Deep sensations: Deep pain, sense of passive movebment, position and vibration.
3. Combined sensations (Syn: Cortical sensation): These are dependent on superficial and deep sensations and interpretation by the sensory cortex. These are two point discrimination, traced figure identification (graphesthesia), stereognosis and appreciation of double, simultaneous stimulation.

Tests for Superficial Sensations

These are touch, superficial pain and temperature.

Touch

- Use a wisp of cotton wool, a piece of thin paper, camel hair brush, or your own finger tip.
- Apply the stimulus gently without deforming the skin, to avoid pressure sensation.
- Start from the face and go down the body up to the feet.



Fig. 32.44: Testing the sense of touch using a hair brush. (*See* text for description)

- Instruct the patient to say 'yes' promptly if he feels the sensation and also to indicate whether the perceived sensation is normal or altered, i.e. increased, decreased or different from the adjacent normal areas or corresponding area on the opposite side.

 Note: The promptness or delay and any inconsistency in his responses
- Map out the extent of the abnormality, proceeding from the abnormal to the normal area (Fig. 32.44).

 Note: Hairy skin is normally more sensitive than nonhairy skin, and certain areas in the body are more sensitive than others, e.g. palms of hands and soles of feet are less sensitive, whereas the tips of the fingers and toes are more sensitive.

Tactile Localization

Keeping his eyes closed, touch the skin and ask him to locate the spot with his finger. Any error by more than 4 to 5 cm in localizing the point should be considered as abnormal. This test is meaningful only when the touch sensation is relatively preserved.

Tactile localization is the most sensitive function of touch and its impairment suggests a lesion in the contralateral parietal cortex.

Terms used to Denote Abnormalities in Touch Perception

Dysesthesia	Perverted feeling to light touch, e.g. burning or tingling sensation.
Anesthesia	Loss of touch sensation

Hypoesthesia	Reduced touch sensation
Hyperesthesia	Increased touch sensation
Topoanesthesia	Loss of tactile localization
Paresthesia	Feeling of abnormal sensation in the absence of any sensory stimulation, e.g. feeling of cold, warmth, tingling, pricking, cracking, itching, etc.

Superficial Pain

Use a sharp pin with a rounded head. Apply the pointed end of the pin to the skin sharply, to produce an unpleasant sensation. Avoid penetration of the skin by pricking directly. Also apply the rounded head of the pin to demonstrate the difference between a sharp pin prick and a blunt sensation.

- Then apply the sharp and blunt ends of the pin randomly and elicit his response to each stimulus with his eyes closed.
- Do not apply the stimuli too quickly or in close proximity to each other, since this may lead to cumulative effect.
- Instruct the patient to say 'yes-sharp' or 'yes-blunt' if he feels the sensation and also to indicate whether the perceived sensation is normal, increased, decreased or altered as compared with the adjacent normal area or corresponding area on the opposite side.

 Note: The promptness or delay and any inconsistency in his responses.
- Map out the extent of the abnormality, in the same way as described for touch (Fig. 32.45).



Fig. 32.45: Testing superficial pain. Note the position of the pin to avoid penetration. (*See* text for details)

Pain Localization

Keeping his eyes closed ask him to locate the area that was pricked. Any error by more than 1 to 2 cm in localizing the prick should be considered as abnormal.

Note: Touch and pain may be affected in lesions of peripheral nerves or spinal cord. In peripheral nerve lesions the area of anesthesia will be greater than the area of analgesia. The reverse occurs in lesions of the spinal cord.

Terms used to Denote Abnormalities in Pain Perception

Analgesia	Loss of pain sensation
Hypoalgesia	Reduced pain sensation
Hyperalgesia	Increased pain sensation
Hyperpathia	Increased pain sensation to stronger pin pricks in an area that has reduced sensation to milder pricks.

Temperature Sensation

- Use hot (about 49–50°C) and cold (about 5–10°C) water in two identical test tubes.
- Apply the test tubes randomly over the skin for less than two seconds each time, with the patient's eyes closed.
- Instruct him to say 'hot' or 'cold' in response to each stimulus.
- Inability to perceive the sensation of hot or cold or inability to differentiate hot from cold or overreaction to these stimuli should be considered abnormal.

Temperature Discrimination

Using water at different temperatures in test tubes, ability to appreciate minor differences can be tested. A normal person should be able to appreciate a difference of 1°C when the water temperature ranges between 28 to 32ºC.

Terms used to Denote Abnormalities in Hot and Cold Sensation

Thermanesthesia	Loss of temperature sensation
Thermhypoesthesia	Reduced temperature sensation
Thermhyperesthesia	Increased temperature sensation

In pathological conditions, the following abnormalities may be observed:

i. Both hot and cold sensations may be affected to the same degree or there may be dissociation in the degree of involvement, one more affected than the other.
ii. Both hot and cold stimuli may be perceived only as 'hot' e.g. in high cervical cord lesions.
iii. When both hot and cold sensations are impaired, the area of impairment for 'hot' will be greater than that for 'cold'.
iv. The border of demarcation between normal and affected areas will be more distinct and consistent when tested for temperature than for pain when both are affected.
v. Dissociated anesthesia, i.e. loss of pain and temperature sensation with preservation of touch and other sensations suggests a lesion near the central canal of the spinal cord where the crossing fibers of the spinothalamic tracts of both sides are selectively involved, e.g. syringomyelia, hematomyelia, intramedullary tumors of the spinal cord and others.

Tests for Deep Sensations

These are deep pain, sense of passive movement, position and vibration. The term 'joint sense' includes sense of passive movement and position.

Deep Pain

Squeeze the Achilles tendon, calf muscles, or the biceps muscle with your hand to produce pain. An alternative method is to hyperflex the fingers forcibly. Normally this evokes a poorly localized, deep, uncomfortable sensation. The alteration in sensation should be gross, to be of diagnostic significance.

Sense of Passive Movement

Explain to the patient that you will be moving passively his great toe or thumb, either up or down and he should respond by saying 'up' or 'down' each time a movement is made and demonstrate the same to him, while he is watching. He should be instructed not to move the digit actively during the test. Though the great toe and thumb are normally chosen, any joint can be tested in this way.

The joint to be tested is fixed proximally by holding it between the left thumb and index finger, so that the movement imparted to the joint is not felt proximally. Hold the sides of the distal phalanx between the thumb and index finger of the right hand and move it up or down randomly. Ask the patient to close his eyes and respond promptly each time the part is moved. Start with greater degrees of movement and gradually reduce the amplitude in order to detect the smallest range of movement that he can appreciate.

A normal person should be able to detect even 1° of movement at the terminal interphalangeal joint of the thumb and the great toe and 10° at other joints.

Inability to perceive the direction of the movements and the movements when they are of small amplitude, and errors in correct perception are all abnormal.

Note: i. The examiner should hold the part to be moved in a position away from the line of movement since the pressure on the part can help to identify the direction of movement even when the sense of position is lost.
ii. The patient should be instructed to say 'up' or 'down' in relation to the previous stationary position of the digit and not in relation to its neutral position (Fig. 32.46).

Sense of Position

Hold one limb in a particular position passively by the examiner. Ask the patient to keep the corresponding limb on the opposite side in the same position initially with eyes open and later with eyes closed.



Fig. 32.46: Testing sense of passive movement. (*See* text for description)

Note: Ability to perform the test with eyes open but not with eyes closed is suggestive of loss of proprioceptive sensation. Sense of passive movement and sense of position have the same significance. However, the former is more commonly tested because it is easier to perform and can be graded. It is also the first modality to be affected in lesions of posterior columns.

Small toe in the foot and little finger in the hand are affected earlier than the great toe or thumb (Fig. 32.47).

Vibration

Use a tuning fork of 128 Hz frequency. Greater frequencies are less easy to perceive.

Demonstrate to the patient the difference in the perception during vibration and after the cessation of vibration of the tuning fork, by firmly applying the base of the fork to his sternum. A vibrating fork gives a buzzy feeling, in addition to the pressure of the fork on the sternum whereas a non-vibrating fork produces only a feeling of pressure. After he has understood the test, the vibrating fork is applied over the following bony prominences starting distally and proceeding towards the proximal parts. Bony points are tested mainly because the bone acts as a resonator of vibration.

Lower limb: Dorsum of the distal phalanx of the big toe, medial and lateral malleoli, tibial tuberosity, anterior superior iliac spine (Fig. 32.48).

Upper limb: Dorsum of distal phalanx of thumb, ulnar and radial styloid process, olecranon and acromion processes.

Vibration over the spinous processes of the vertebrae can also be tested.

Ask him whether he feels the vibration of the fork or not. If he says yes, ask him to indicate promptly when that feeling stops. Transfer the fork immediately to the corresponding area on the opposite side and enquire whether he feels the buzzing sensation at that location. Duration of vibration at a given site can also be compared with that of the examiner.

Inability to perceive the sense of vibration or reduction in the duration of perception compared to the normal side, are abnormal. Absence of vibration sense only in the distal parts of the limbs suggests lesion in peripheral nerves. If uniform loss occurs below a certain level, it suggests lesion in the spinal cord. When the loss of vibration is confined to one side of the forehead, sternum or symphysis pubis it suggests hysterical reaction. In peripheral nerve lesions, loss of vibration occurs earlier than other modalities of sensation. Dissociation between vibration sense and joint sense may occur in some spinal cord lesions. Lesions above the thalamus usually do not affect the sense of vibration. Hence, in parietal lobe lesions vibration sense may be intact whereas the joint sense is affected on the opposite side.



Fig. 32.47: Testing sense of position. The patient is made to hold the corresponding part of the opposite limb (arrow) in the same position held by the examiner (*See* text for description)



Fig. 32.48: Testing sense of vibration over the medial malleolus. The intensity of stimulus can be varied and tested. (*See* text for description)

Tests for Combined Sensations

These are two point discrimination, traced figure identification, stereognosis and double simultaneous stimulation.

Note: These tests should be carried out only when the superficial and deep sensations are relatively preserved.

Two Points Discrimination

Use a caliper or a compass divider. Demonstrate to the patient the difference between one point and two points stimulation.

Keeping his eyes closed, apply the two points of the caliper or divider with equal pressure simultaneously on the following areas:

Lips, dorsum of the hand, finger tips and dorsum of the foot. By varying the distance between the two points of the caliper, note the minimum distance required, for him to perceive the stimulus as two in the above areas.

Test the corresponding sites on the two sides maintaining the same relationship between the two points of the caliper and the long axis of the limb.

A normal individual should identify a minimum distance of 2 to 3 mm on the lips, 2 to 3 cm on the dorsum of the hand, 3 to 5 mm on finger tips and 3 to 4 cm on the dorsum of the foot. Two point discrimination is lost in contralateral parietal lobe lesions.

Traced-Figure Identification

Use a pencil, key or the pointed end of percussion hammer.

After explaining and demonstrating to the patient, draw firmly and slowly on the skin of the palm or dorsum of the foot a single digit (0–9) exceeding 4 cm in size or an alphabet letter familiar to him and ask him to identify the same, with his eyes closed.

While drawing on the skin, stand by the side of the patient, facing the area to be tested, so that the drawn figures will be more easily recognized by the patient.

Compare the corresponding areas on the two sides of the body. Inability to recognize the traced figures correctly is abnormal and is called graphesthesia. It is suggestive of a lesion in the contralateral parietal lobe.

Stereognosis

It is the ability to identify an object by handling it. In addition to the relatively preserved superficial and deep sensations, this test also requires sufficient power in the muscles of the hand to move and manipulate the object. Explain to the patient that he is required to identify the object placed in his hand by its feel only and not by looking at it.

Keeping his eyes closed, place common objects one at a time, such as coins of various sizes, pen, watch, paperweight or a key, in his hand and ask him to identify the object (Fig. 32.49). The test may be repeated with different objects familiar to the patient. Failure to identify is more important in evaluation.

Unlike all other sensations, this sensation is tested without prior demonstration and the abnormal side is tested first. Otherwise he may remember the object shown to him or identified by the normal side and from that memory, he may tell correctly when the affected side is tested.

Inability to identify the objects or delay in identification is abnormal and this is called astereognosis. It occurs in lesions of the contralateral parietal lobe.

Double Simultaneous Stimulation

It is the ability to perceive two identical stimuli, applied, simultaneously on both sides of the body in corresponding areas.

Use the tips of your two index fingers or two equally sharp pins, to deliver the two stimuli.



Fig. 32.49: Testing stereognosis with a paperweight. (*See* text for details)



Fig. 32.50: Testing for sensory inattention. Two stimuli are applied simultaneously at identical points on either sides. (*See* arrowheads)

Explain to the patient that you will be applying the stimulus either on one side, or both sides simultaneously. He should respond by saying 'one' or 'two' as the case may be. If he feels only 'one' he should indicate the side.

Keeping his eyes closed, apply the stimuli randomly to one or both sides with equal pressure and note his response.

Inability to perceive simultaneously applied stimuli as two is abnormal even through he is able to perceive each stimulus separately when applied to the same areas. This is called sensory extinction or inattention. (Syn: sensory suppression, repression, eclipse, rivalry). It occurs in lesions of the contralateral parietal lobe. It may be the only sensory abnormality in some cases with parietal lobe lesion. (Fig. 32.50).

CO-ORDINATION

For proper smooth and harmonious performance of a movement, motor, sensory and synergizing functions should operate normally. For this, sensations, especially proprioception should be intact, the agonist muscles should contract normally, their antagonists should relax to facilitate the agonists, the synergistic muscles should assist the prime movers, and the fixating muscles should fix the proximal joints and the limbs. The cerebellum should coordinate all these movements. Only when all these structures are intact, the attempted movement will be properly coordinated. Clinical tests for coordination are directed to assess particularly the functions of cerebellum and proprioceptive pathways.

Co-ordination is of two types:

i. The equilibratory co-ordination required for the maintenance of balance and posture. Examination of stance and gait includes tests for equilibratory co-ordination.
ii. Nonequilibratory co-ordination required for the execution of voluntary limb movements.

Tests for Nonequilibratory Co-ordination

Upper Limbs

Finger-nose test: The patient should be in sitting or standing position. Instruct him to abduct and, extend one upper limb completely to horizontal position and then touch the tip of his nose with the palmar aspect of the tip of his index finger

Guidelines to Localize the Site of Lesion Based on Sensory Abnormalities

Sensory loss	*Site of lesion*
1. Loss of all sensations in a restricted area. Sensory loss conforms to the distribution of root or peripheral nerve	Spinal root or peripheral nerve lesion
2. Loss of sensations in glove and stocking distribution, i.e. distal parts of all four limbs	Peripheral polyneuropathy
3. Saddle anesthesia (perianal region) lesion	Conus medullaris or cauda equina
4. Loss of all sensations below a definite level on the trunk on both sides	Spinal cord—total transection
5. Loss of pain and temperature sensation with preservation of joint and vibration sense below a definite level on the trunk on both sides	Spinal cord anterior lesion, e.g. anterior spinal artery thrombosis, multiple sclerosis
6. Loss of joint and vibration sense with preservation of pain and temperature below a level on the trunk on both sides	Spinal cord—posterior lesion, e.g. tabes dorsalis

Contd...

Contd...

Sensory loss	Site of lesion
7. Loss of pain and temperature sense on one side and vibration and joint sense on the opposite side below a definite level on the trunk	Spinal cord—hemisection on the side of loss of joint and vibration sense
8. Dissociated, anesthesia, i.e. loss of pain and temperature sensation with other sensations preserved over a band of skin on the trunk on both sides with normal sensations above and below that band	Spinal cord—central lesion, e.g. syringomyelia, hematomyelia, and intramedullary tumor
9. Loss of pain and temperature sensation on one side of face and contralateral side of the body	Lateral aspect of medulla oblongata on the side of affection of the face, e.g. lateral medullary syndrome
10. Unilateral loss of all sensations on one side of the body including face. Position sense more frequently affected than others. Deep sensations more affected than superficial sensations	Thalamic lesion of the opposite side
11. Relatively preserved superficial and deep sensations with abnormalities in two-point discrimination, stereognosis, graphesthesia, and sensory extinction	Parietal lobe lesion of the opposite side
12. Loss of touch and pain sense extending exactly up to the midline over the face and trunk; loss of vibration sense only on one side of the forehead, sternum or symphysis pubis; Bizarre sensory loss not conforming to any organic pattern	All these suggest hysterical conversion reaction

first slowly and then rapidly, initially with his eyes open and then closed. Make him do this several times in different angles and at different planes. The two sides are tested separately. While he is doing so, observe the speed, smoothness, rate, range, direction and force of movement of the index finger. Normally the movement of the finger will be smooth, regular, rhythmic and precise (Figs 32.51A and B).

In cerebellar lesion which also produce in coordination the following differences may be seen:

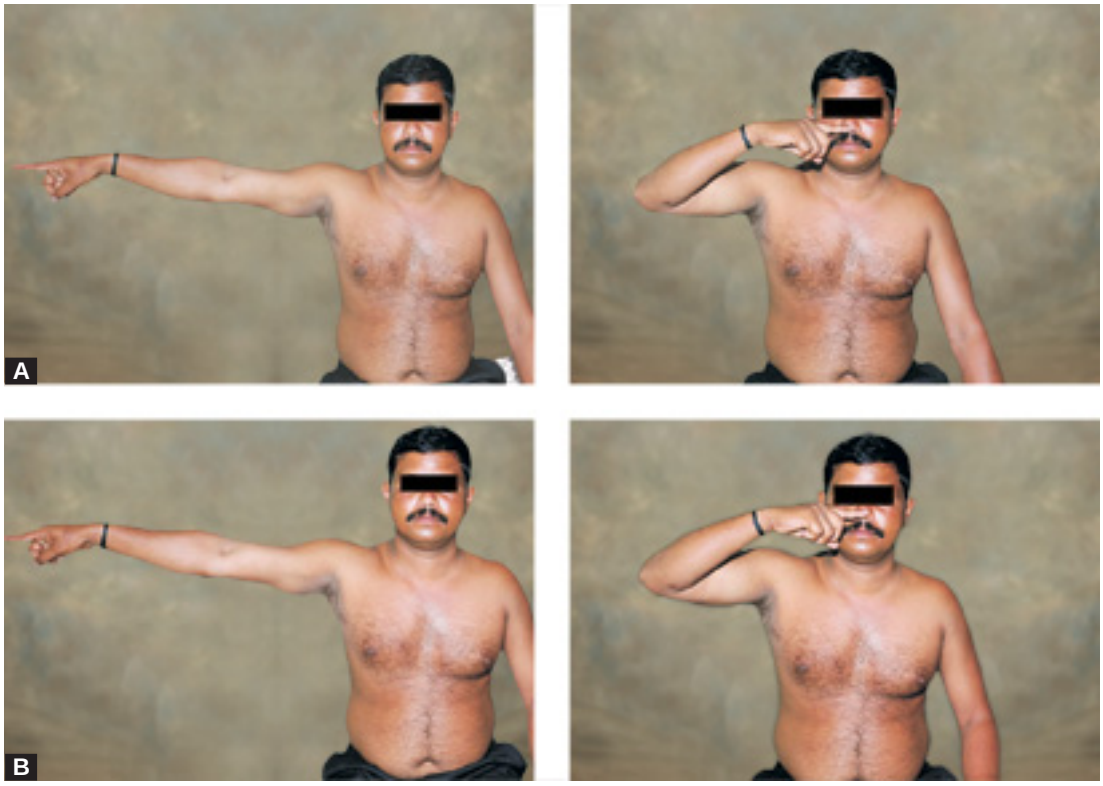
i. There will be coarse and irregular tremor as the finger approaches the nose—'intention tremors'
ii. The finger may stop short of his nose—hypometria
iii. It may touch the nose with too much speed and force or it may overshoot the nose and touch the cheek—hypermetria
iv. The tip of the finger may consistently deviate to the side of lesion.

All these abnormalities will be noticed irrespective of whether the test is performed with eyes open or closed, in the limb ipsilateral to the cerebellar lesion.

Minimal or latent ataxia can be brought out by applying slight resistance with two fingers of the examiner on the ventral surface of the patient's wrist or forearm while he is doing the test.

In sensory ataxia due to loss of proprioception, the abnormalities will be apparent in the affected limb only when the test is performed with eyes closed.

Nose-finger-nose test: The patient is asked to touch with the palmar aspect of the tip of his index finger the tip of his nose and then the tip of the index finger of the examiner held in front, alternately and rapidly, several times. The examiner shifts his finger to different positions within the reach of the patient. To bring out the tremors fully the patient's hand has to be abducted and extended fully. Both sides are tested separately.



Figs 32.51A and B: Finger nose test (A) With eyes opens, (B) With eyes closed

Observations and significance are the same as for finger-nose test, but this test is more sensitive.

Rapid Alternating Movements (Diadochokinesis)

The patient is asked to alternately pronate and supinate the forearm rapidly, with his elbow flexed to 90° and tucked to the side of the chest. Both sides are tested separately. In cerebellar dysfunction this will be defective and clumsy on the ipsilateral side—dysdiadochokinesia (Figs 32.52 A and B) Even in normal persons, minor differences may occur in the nondominant hand.

Finger wiggle test: Keeping the upper limb relaxed and partially outstretched in front, the patient is instructed to wiggle his fingers (short quick irregular movements) up and down, as demonstrated to him by the examiner. The rate, rhythm, range and speed of the finger movements are observed. The test is performed first on one side and then on the other. Even in normal persons minor differences may occur on the nondominant hand.

In cerebellar diseases, the rate of finger wiggling will be slow and the rhythm and range will be irregular. In rigidity due to extrapyramidal disorders the rate will be slow and the range of the finger movements gradually diminish after a few movements. In spasticity also the rate will be slow.

This is a sensitive test to detect minor cerebellar, pyramidal and extrapyramidal dysfunction, especially when other tests for motor power, tone, coordination and muscle stretch reflexes are all grossly normal.

Pointing test: With the patient in sitting or standing position, he is asked to outstretch his upper limb in front of him and then touch the tip of the examiner's index finger held in front of the patient, using his index finger. Then he is asked to raise his upper limb vertically up and bring it down to touch the examiner's index finger again and again. This should be done several times, first with eyes open and then closed. The two sides are tested separately.

A normal individual can do this test with ease and precision. In unilateral cerebellar lesion, the



Figs 32.52A and B: Rapid alternating movements to test cerebellar function. Diadochokinesis. (*See* text for details)

finger of the ipsilateral hand always deviates towards the affected side. In unilateral vestibular lesion, the fingers of the ipsilateral as well as the contralateral hand deviate towards the affected side.

The deviation will be more marked with the eyes closed. In sensory ataxia, the test will be normally performed with the eyes open, but with eyes closed, the finger deviates in different directions.

Weight assessment: Objects of different weights but almost of same size are placed in one hand held in front, one at a time and the patient is asked to tell with his eyes closed, which object weighs more. The test is carried out separately on both sides. A normal individual can distinguish minor differences in weights when small objects are used whereas a patient with cerebellar disease cannot do so on the affected side.

Handwriting: When the patient with a cerebellar disease is made to write, the letters tend to become larger, especially at the end of words or sentences. This is called megalographia. In parkinsonism, the opposite phenomenon may be noted, i.e. micrographia.

Rebound phenomenon: Keeping the arm adducted at the shoulder, forearm supinated and semiflexed at the elbow and the hand made into a fist, the patient is asked to bend the forearm against resistance applied by the examiner. The other hand of the examiner protects the face of the patient from being hit by the uncontrolled flexion of the elbow. While the patient is forcibly flexing his forearm the examiner suddenly releases the resistance. In normal individuals, the triceps muscle contracts immediately and this arrests further flexion of the forearm. In a patient with cerebellar disease, the checking force of triceps is inadequate so that the patient's forearm continues to flex and may even hit his face (positive rebound phenomenon).

Alternate method: The patient holds his upper limb outstretched horizontally in front. The examiner presses the distal part of the forearm to displace it down while the patient resists it and suddenly the examiner removes his hand. In normal persons the forearm which is displaced down by the push returns to its original position promptly. In unilateral cerebellar disease, the ipsilateral limb rebounds up excessively. Sometimes, the rebound phenomenon may be present in a spastic limb as well.

Lower Limbs

Heel-knee test: The patient lies in bed with both lower extremities straight. He is then asked to place the heel of one foot on the opposite knee and smoothly slide it down along the shin and over the dorsum of the foot towards the big toe. Then he has to lift the heel up and bring it back to the knee again and repeat this procedure three or four times,





Figs 32.53A and B: Heel-knee test for co-ordination (arrows)

first looking at the legs and then with eyes closed. The rate, range, smoothness, direction and force of movement of the heel are noted. The test (Figs 32.53A and B) is repeated on the other side. A normal individual performs this act smoothly, rapidly and with precision. In unilateral cerebellar lesion, the movement of the ipsilateral leg will be slow, clumsy and irregular in rate, rhythm and range both with eyes open as well as closed. In sensory ataxia the test can be done well with eyes open, but it becomes clumsy with eyes closed.

Toe-finger test: The patient who lies in bed is asked to touch with his great toe the tip of the examiner's finger or any other object held steady about 60 cm above the bed within reach. The test is repeated several times while the examiner shifts his finger or the object to different positions. The two sides are compared for the speed, range and direction of movement of the toe. Interpretation of findings is the same as for heel-knee test (Fig. 32.54).



Fig. 32.54: Test for co-ordination (Toe-finger test)

Foot Pat Test

The patient is made to sit on a chair which his feet touching the floor flat. He is asked to pat the floor rhythmically and rapidly with his forefoot. Both sides are tested separately. The rate, rhythm, and speed of the patting movements are compared on both sides. If the patient is unable to sit up, the test is performed in supine position by asking the patient to pat the foot on the examiner's palm or the foot board of the bed. Even minimal cerebellar lesions can be detected by this test.

Note:

1. All tests for coordination may be abnormal or less accurate, if there is paresis, rigidity, spasticity or involuntary movements in a limb. But this is not called in coordination.
2. Incoordination applies to cerebellar or proprioceptive deficits.
3. Incoordination or ataxia is of two types:
 i. *Static ataxia:* When a limb is outstretched horizontally it sways or oscillates up and down, and
 ii. *Kinetic or motor ataxia:* Incoordination occurs only during movement.

The first type occurs in advanced disease while the second type occurs in early stage.

PHYSICAL SIGNS OF CEREBELLAR DYSFUNCTION

The following features are characteristic of cerebellar dysfunction:

i. Hypotonia
ii. Postural changes of the head, i.e. the head is rotated and flexed with the shoulder at a lower level than the opposite normal side.

iii. Wide-based, ataxic gait
iv. Incoordination of voluntary movements, i.e. finger-nose and heel-knee ataxia
v. Dysdiadochokinesis, i.e. inability to perform rapid, alternate movements of the limbs
vi. Intention tremors
vii. Pendular knee jerk. With the subject sitting at the edge of the bed and legs hanging down freely, elicit the knee jerk. There will be a series of jerky oscillatory movements of the legs (usually more than three) before it comes to a halt. Normally, these to and fro movements are prevented due to the aftershortening of the quadriceps muscle. In cerebellar lesions, due to hypotonia of the flexor and extensor muscles of the leg and due to lack to restraining effect which they normally exert on each other, the reflex becomes pendular.
viii. Nystagmus
ix. Dysarthria.

In pure cerebellar lesions, there is no muscle paralysis or atrophy and no sensory changes. In acute cerebellar lesions, the clinical features of cerebellar dysfunction will be sudden and severe, whereas in chronic lesions the symptoms and signs are less severe and slow to develop.

In lesions of the vermis which is a midline structure, the motor incoordination mainly involves the axial musculature (head, neck and trunk) rather than the appendicular (limb) musculature. Hence, there will be difficulty in holding the head steady and the trunk erect with a tendency to fall forwards or backwards-trunk ataxia.

Lesions of cerebellar hemispheres usually produce features of cerebellar dysfunction only in the ipsilateral limbs, especially in the upper limb, with a tendency to sway and fall towards the side of lesion. Dysarthria and nystagmus are also common in cerebellar lesions.

SIGNS OF MENINGEAL IRRITATION

These include neck rigidity (Fig. 32.55), Kernig's sign (Fig. 32.56) and Brudzinski's signs. These develop when the leptomeninges are inflamed as in meningitis, or irritated as in subarachnoid hemorrhage.

a. *Neck rigidity:* It may be defined as the resistance to passive flexion of the neck unassociated with a local painful condition. Normally the neck is supple and can be easily flexed passively so that the chin touches the sternum. In the presence of neck rigidity flexion of the neck is difficult and painful. With extreme grades of neck rigidity the neck may be held in the hyperextended position with backward arching of the trunk, i.e. opisthotonos. This sign used to be seen in children with tuberculous meningitis and syphilitic basal meningitis.



Fig. 32.55: Test for neck rigidity. Flex the neck passively and also turn it from side to side while the patient is fully relaxed. Look for resistance to flexion and other movements



Fig. 32.56: Kernig's sign—Flex the knee to a right angle and straighten the leg as shown (*See* text for description)

b. *Kernig's sign:* This test is to assess the spasm of the hamstring muscles and response to stretch of the sciatic nerve. The patient lies supine. The examiner standing by the side, passively flexes the hip and knee to right angles and then straightens the leg. Normally this is a painless procedure, though in the elderly it may be slightly uncomfortable. Painful spasm restricting extension of the knee is positive Kernig's sign.

This is repeated on the other side as well. While eliciting the Kernig's sign, watch the patient's face for expression of pain, and observe the other knee for automatic flexion.

c. *Brudzinski's signs*
 i. *Leg sign:* While eliciting the Kernig's sign on one side the opposite lower limb flexes automatically.
 ii. *Neck sign:* While eliciting neck rigidity, both the lower limbs flex automatically.

Based on the clinical findings the investigations are determined.

INNERVATION OF URINARY BLADDER AND DISORDERS OF MICTURITION

Disturbances of micturition are common and often they are early manifestations in some neurological disorders. Lesions of the spinal cord and cauda equina, and less commonly cerebral disorders give rise to abnormalities of micturition.

Innervation of the Urinary Bladder

The urinary bladder is a hollow sac of smooth muscle with two sphincters at its opening into the urethra—one internal and one external. The wall of the bladder contains detrusor muscle which contracts to empty the bladder. The internal sphincter is made up of smooth muscle fibers arranged in such a way that their contraction opens the sphincter. The detrusor and internal sphincter are not under voluntary control. The external sphincter contains striated muscle fibers, and its contraction and relaxation are under voluntary control. The neural control of the bladder and its sphincters is complex. It has a dual efferent nerve supply both from parasympathetic and sympathetic. The parasympathetic efferent innervation is from the intermediolateral zone of gray matter of S2,3,4 spinal segments. Their postganglionic fibers innervate the detrusor muscle and internal sphincter. Parasympathetic stimulation leads to contraction of detrusor muscle and internal sphincter, resulting in emptying of the bladder. The external sphincter is supplied by somatic efferent fibers that arise from S2,3,4 spinal segments (Onuf's nucleus) and travel in the pudendal nerves.

The bladder also receives sympathetic innervation from L1,2 spinal segments via the hypogastric plexus, but its exact role in micturition is not fully known. Sensations arising from the bladder are carried up by somatic and visceral afferent nerves (pelvic and hypogastric nerves). Sensory impulses from the pressure receptors situated in the bladder wall ascend up to enter the S2,3,4 spinal segments and these convey the sensation of bladder distention whereas the visceral afferent fibers from the peritoneal surface of the bladder enter the lower portion of the thoracic spinal cord to convey a sense of bladder fullness. Sensations from the urethra and external sphincter are carried by the pudendal nerves to S3,4 spinal segment.

Note: Several local diseases affecting the lower urinary tract lead to retention and/or incontinence and other urinary symptoms that are associated with neurogenic bladder. All these should be excluded before attributing bladder dysfunction to a neurological cause.

Act of Micturition

The complex act of micturition is both reflex and voluntary. Pressure receptors in the bladder wall send afferent impulses to S2,3,4 spinal segments and this forms the afferent mechanism for the micturition reflex.

During micturition, the following actions take place sequentially:

- Relaxation of the perineal musculature
- Increase in the tension of the anterior abdominal wall
- Contraction of detrusor muscle and internal sphincter
- Relaxation of the external sphincter
- Voiding of urine.

Voluntary contraction of the external sphincter and the perineal muscles causes cessation of the contraction of the detrusor muscle and stopping

of micturition. Voluntary control on the bladder is exercised by the paracentral motor region of the frontal cortex, via the descending fibers that lie anteriorly in the corticospinal tracts in the spinal cord, to reach the anterior horn cells of the S2,3,4 spinal segments. In spinal cord compression these fibers get compressed early and this explains the bladder disturbances that occur in cord compression.

Other central mechanisms in the brainstem may also play a role in micturition, but their exact nature is not clear. The action of pyramidal fibers is to inhibit the lower motor neurons of the sacral segments of the spinal cord. By varying this inhibitory effect voluntarily, one can initiate and stop micturition at will. A normal child usually gains control of micturition during day time by 2 years and at night, by 3 years of age. However, considerable variations occur in normals.

Abnormalities of Micturition

Any lesion in the neural pathway concerned with micturition may result in bladder dysfunction (neurogenic bladder). There are mainly six types of neurogenic bladder disturbances (Fig. 32.57).

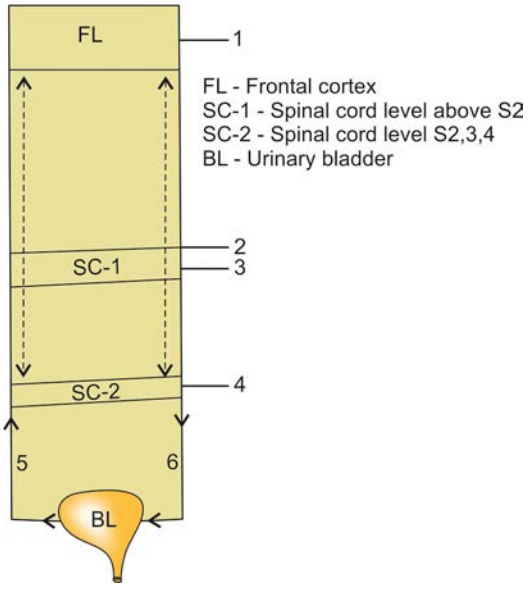


Fig. 32.57: Diagram showing the levels of lesion and types of dysfunction in neurogenic bladder: (1) Uninhibited bladder, (2) Atonic bladder (Acute stage), (3) Automatic bladder (Chronic stage), (4) Autonomous bladder, (5) Sensory bladder and (6) Motor paralytic bladder

They are:

i. Uninhibited bladder.
ii. Atonic bladder.
iii. Automatic bladder.
iv. Autonomous bladder.
v. Sensory bladder.
vi. Motor paralytic bladder.

The characteristic features of these six types are shown in Tables 32.19 and 32.20.

Neurogenic bladder never occurs in primary muscle diseases, lesions of the neuromuscular junction and primary psychiatric illnesses. Unilaterally lesions of the central nervous system or cauda equina usually do not result in bladder dysfunction, unless pressure effects occur over the opposite side as well, or the condition is acute. Only bilateral lesions produce persistent neurogenic bladder. Acute or subacute bilateral lesions are more prone to result in bladder dysfunction.

Whenever neurogenic bladder dysfunction is suspected, a detailed neurological examination should be carried out, particularly to detect the presence and pattern of the sensory impairment in the perianal region which is a common accompaniment of cauda equina lesions. The spine in the lumbosacral region should be carefully examined for deformities, tenderness, swelling, tuft of hair, sacral dimple or sinus in the skin, since these may be the external markers of the underlying pathology in the nervous system.

Clinical Symptomatology in Neurogenic Bladder

The following symptoms may occur to a variable degree, in different types of neurogenic bladder (Table 32.20).

Frequency

It is the number of times the bladder is emptied in a day. A normal adult empties his bladder up to 3 to 6 times during day and upto 2 to 3 times during night.

Urgency

Once the sensation of distension of bladder is perceived, the patient finds it difficult to hold the

Table 32.19: Types of neurogenic bladder and their characteristic features

	Uninhibited bladder	*Atonic bladder*	*Automatic bladder*	*Autonomous bladder*	*Sensory bladder*	*Motor paralytic bladder*
Site of lesion	Frontal lobe	Spinal cord above S2 acute stage	Spinal cord above S2 chronic stage	Spinal S2,3,4 segments/cauda equina roots S2,3,4	Posterior spinal roots-S2,3,4, or posterior columns	Anterior spinal S2,3,4 roots
Clinical features:						
Bladder sensation	Present	Absent	May or may not be present	Absent	Absent	Present
Bladder evacuation	Sudden	Overflow incontinence	Sudden complete reflex evacuation once in 1-4 hours	Overflow incontinence	Overflow incontinence	Overflow incontinence
Bladder distension	May or may not be present	Present	Absent	Present	Present	Present
Bladder capacity	Variable	Increased	Small	Slightly increased	Markedly increased	Variable
Bladder control (initiation and inhibition)	Lost	Lost	Possible but difficult	Lost	Possible on straining	Lost
Urine volume with each evacuation	May be small or large	Small	Small	Small (less than 250 ml)	Large (in liters)	Small
Urine stream	Normal	Dribbling	Normal	Dribbling	Dribbling	Dribbling
Residual urine	Nil	Large	Nil	Large	Large	Variable
Realization of having passed urine	Absent	Present	Present	Present	Present	Present

Note: Several local diseases affecting the lower urinary tract lead to retention and, or incontinence and other urinary symptoms that are associated with neurogenic bladder. All these should be excluded before attributing bladder dysfunction to a neurological cause.

Table 32.20: Clinical symptomatology in different types of neurogenic bladder

Symptoms	*Uninhibited bladder*	*Atonic bladder*	*Automatic bladder*	*Autonomous bladder*	*Sensory bladder*	*Motor paralytic bladder*
Frequency	I	R	I	±	R	+
Urgency	+	—	+	—	—	+
Incontinence						
(a) Dribbling	—	+	—	+	+	+
(b) Massive	+		+			
Hesitancy	—	+	+	+	+	+
Distention and retention	±	+	—	+	+	+
Desire to void	Normal	Lost	Lost	Lost	Lost	Normal
+ = Present	— = Absent	± = Variable	R = Reduced	I = Increased		

urine any longer and micturition becomes urgent or precipitant.

Incontinence

It is the inability to control voiding of urine voluntarily. The urine is voided involuntarily either as a continuous stream (massive incontinence) or in intermittent drops (dribbling incontinence).

Hesitancy

Once there is a desire and attempt to pass urine, there is delay or difficulty in starting the act of micturition.

Distension

It is an abnormal increase in the capacity of the bladder to hold urine.

Retention

Due to incomplete emptying of the bladder, urine accumulates in the bladder.

Diseases in which Different Types of Neurogenic Bladder Occur

Uninhibited Bladder

The voluntary inhibitory control is abolished. Hence the patient urinates in inappropriate places without realizing that he has done so, e.g. frontal lobe lesions, mental retardation, dementia, cerebral palsy.

Atonic Bladder

The bladder and its sphincters lose their tone and ability to contract, e.g. acute stages of transverse myelitis, cord compression, cord trauma, vascular lesion of the spinal cord and multiple sclerosis. As the condition becomes chronic, automatic bladder develops in them.

Automatic bladder (Syn: UMN type bladder, small contracted bladder, reflex bladder). The bladder automatically evacuates as soon as small amount of urine collects in it. This occurs when the lower reflex arc of micturition is intact, but its higher control is abolished, e.g. chronic stages of transverse myelitis, spinal cord compression and trauma, vascular lesion of the spinal cord and multiple sclerosis.

Autonomous Bladder

The bladder does not contract reflexly. It gets distended and urine dribbles. This occurs in traumatic lesions and tumors of the sacral spinal cord and spina bifida.

Sensory Bladder

The afferent sensations from the bladder to the brain are abolished. This occurs in diabetic autonomic neuropathy, tabes dorsalis, multiple sclerosis and others.

Motor Paralytic Bladder

The afferent pathways and sacral cord segments are intact, but the efferent pathway of the reflex arc is damaged. This occurs in polyradiculoneuritis, trauma and tumors of cauda equina, and spina bifida.

NERVOUS CONTROL OF THE RECTUM AND DEFECATION REFLEX

The act of defecation is also a coordinated reflex like micturition, resulting in the emptying of the descending and pelvic colon, rectum and anal canal. The innervation of the rectum and anal canal is similar to that of the bladder. The internal sphincter of the anal canal is not under voluntary control. It is supplied by the postganglionic sympathetic fibers from the pelvic and hypogastric plexuses (T11–12). They are responsible for its contraction. The external sphincter of the anal canal is under voluntary control. It is innervated by the inferior rectal nerve. Stimulation of the stretch receptors in the wall of the rectum initiates the act of defecation which is assisted by a rise in the intra-abdominal pressure brought about by contraction of the muscles of the abdominal wall.

In lesions of the spinal cord above S2 level, urgency and precipitancy of defecation develop. Lesions of the sacral segments of the spinal cord result in hypotonia and distension of the colon, laxness of the anal sphincter, loss of anal reflex in both sexes and in males, loss of bulbocavernous reflex as well. Because of the common nerve supply, quite often double incontinence of bowel and bladder occurs in spinal cord lesions, the urinary symptoms being more prominent.

Normal child can express the urge to go to toilet by the age of 1½ years and by 2 years it gains control over defecation.

NEURAL CONTROL OF SEXUAL FUNCTION IN MALE

Penile erection and ejaculation are two components of the sexual function in the male.

Erection of the penis (potency) is controlled by the parasympathetic nerve fibers from S2,3,4 spinal segments, which are under the influence of the reticulospinal tracts from above. Acute lesions of the spinal cord above S2 level result in loss of erection. Later, after the period of spinal shock is over, spontaneous or reflex erection may return if the sacral segments are intact. This is called priapism.

Ejaculation of semen from the seminal vesicles into the prostatic urethra is controlled by the

sympathetic nerve fibers from L1,2 spinal segments. Final ejaculation of semen from the penis occurs as a result of the rhythmic contraction of the bulbospongiosus muscles which are innervated by the pudendal nerve (S2,3,4).

Though the acts of penile erection and ejaculation are autonomic reflexes, they are heavily influenced by psychic factors, supraspinal descending neural pathways and hormonal factors. Organic lesions of the spinal cord and cauda equina may lead to impotence. Autonomic neuropathy due to several causes may aslo result in impotence. When only the sympathetic nerve supply from L1,2 spinal segments is affected, normal erection may still occur but ejaculatory failure is present.

The term libido refers to sexual impulse, drive or desire. This results from a variety of stimuli including purely imaginary ones, which arise in neocortex and travel to sacral spinal centers via limbic system and the hypothalamus.

Neurological lesions giving rise to abnormal - ities in penile erection and ejaculation:

- Lesions of parasympathetic pathways- Impotence due to failure of erection and ejaculation
- Overactivity of parasympathetic pathways Priapism
- Lesions of sympathetic pathways—Failure of ejaculation with normal erection
- Overactivity of sympathetic pathway—Weak erection and premature ejaculation

Priapism occurs in lesions of spinal cord above lumbar level or due to overstimulation of parasympathetic pathways. It may occur either spontaneously or as a reflex response to even mild stimulation of the penis resulting in erection and ejaculation.

TESTS FOR AUTONOMIC FUNCTION (TABLE 32.21)

Tests for autonomic function are undertaken when this system is affected either primarily like in Shy-Drager syndrome or secondarily like in diabetes mellitus. Assessment of autonomic functions is of importance to diagnose neurological disorders and also to assess the prognosis in systemic diseases. For example, presence of autonomic neuropathy in diabetes mellitus is associated with a high risk of fatal cardiac arrhythmias.

Table 32.21: Clinical tests of autonomic functions

Test	*Method*	*Expected normal response*	*Abnormal response*	*Remarks*
1. Heart rate response to standing	Record the pulse or heart rate in the supine posture and repeat the measurement in the erect posture or at 60° head-up tilt position in the bed	Increase in heart rate of 14-25 beats/minute as a result of sympathetic stimulation	No increase in heart rate	This is a test for sympathetic efferent vasomotor response. Patients with postural hypotension due to neurogenic cause have abolition of the response while patients of postural hypotension due to non-neurogenic causes like volume depletion will have excessive tachycardia
2. Blood pressure response to standing	Record the BP in the supine posture and repeat the measurement in the erect posture or at 60° after 3 minutes head-up tilt position in the bed	No change in BP	Decrease in the standing BP of atleast 25 mm Hg systolic and 10 mm Hg diastolic (postural hypotension)	This is a test for sympathetic efferent vasomotor activity. Postural hypotension may be symptomatic or asymptomatic
3. Heart rate and BP response to Valsalva maneuver	i. The subject is asked to exhale after a deep inspiration into a manometer or against closed glottis for 10-15 seconds. Heart rate and BP are recorded before, during and after the maneuver	Increasing heart rate for the 10 seconds of sustained forced expiration. BP falls initially (phase 1) but this ceases to fall after the first few seconds (phase 2). After release from blowing, there is a brief period of BP fall (phase 3) followed	Continued fall of BP during phase 2 and neither BP overshoot nor bradycardia during phase 4.	This is a test for sympathetic efferent vasomotor response. Congestive heart failure and chronic obstructive airway disease may influence this test

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Test	Method	Expected normal response	Abnormal response	Remarks
	ii. Record the maximum heart rate in phase 2 and minimum heart rate in phase 4 and find out the ratio of maximum to minimum heart rates	by BP overshoot (phase 4) and a reflex bradycardia. Ratio of more than 1	Ratio of less than 1	
4. Heart rate response to deep breathing	Record the heart rate during quiet breathing and during deep breathing	Sinus arrhythmia	No sinus arrhythmia	This is a test for efferent vagus pathway
5. Heart rate and BP response to carotid sinus massage	Record the heart rate and BP before and during massage of carotid sinus in the neck, first on one side and then on the other side	Bradycardia and fall in BP	No response	This is a test for vagal efferent pathway to heart. Caution is necessary in subjects with hypersensitive carotid sinuses
6. BP response to hyperventilation	Record the BP before and after hyperventilation for 30 seconds	Fall of BP by at least 20 mm Hg systolic	No response or reduced response	This is a test for central integrative function of autonomic nervous system
7. Hand grip test	Record heart rate and BP before and during hand grip for 90 seconds	Increase in heart rate and systolic BP	No response	This is a test for sympathetic efferent pathway
8. Mental arithmetic test	Record heart rate and BP before and during rapid, serial subtractions of 7 from 100	Increase in heart rate and systolic BP	No response	This is a test for sympathetic efferent pathway
9. Cold pressor test	Record heart rate and BP before and during immersion of one hand in a water bath at 4°C for 60-90 seconds	Increase in the heart rate and in systolic BP of at least 15 mm Hg	No response	This is a test for sympathetic efferent pathway
10. Sweat test	Warm the subject either by covering him with blankets or exposing him to a heating lamp so as to increase his rectal temperature by 0.5 to 1°C. Hot tea may be given as a diaphoretic. A chemical powder such as quinizarin is applied to the skin. If the skin is dry, this powder remains grey and if it is moist by sweat, it turns purple	Diffuse sweating	Absence of sweating	This is a test for sympathetic efferent pathway to the skin sweat glands
11. Schirmer's test for tears	Take a piece of thin filter paper (5 mm x 25 mm) and insert one end of it into lower conjunctival sac while the other end hangs over the edge of the lower eyelid	After 5 minutes, the filter paper becomes moist over a length of 15 mm.	Values ofless than 10 mm length of moisture on the filter paper	Note: This can be abnormal due to local causes
12. Pupil response to chemical agents: (a) Epinephrine test	Observe the size of the pupils before and after instillation of 3 drops of 1:1000 epinephrine into the conjunctival sac of both eyes, 3 times within	No response	Pupillary dilatation	This tests the super sensitivity of sympathetically denervated pupil. Incomplete denervation and lesions of central sympathetic pathway do not produce this response

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Test	Method	Expected normal response	Abnormal response	Remarks
	an interval of 3 minutes. Size of the pupils should be noted after 15, 30 and 45 minutes			Responses will be greater in postganglionic efferent lesions than in preganglionic lesions
(b) Cocaine test	4% cocaine solution is instilled into the eyes and the test is carried out as for epinephrine	Pupillary dilatation	No response in pre and postganglionic sympathetic efferent lesions. Slight dilatation of pupils in central sympathetic lesions	A more reliable test for determining sympathetic denervation of pupils
(c) Metha-choline test	2.5% methacholine solution is instilled into the eyes and the test is carried out as above	No response	Pupillary constriction	Suggests parasympathetic denervation of pupils

TESTING: POWER OF MUSCLE

Trunk Muscles (Figs 32.58 and 32.59)



Fig. 32.58: Testing the strength of neck flexors and abdominal muscles. The patient is asked to flex the neck against resistance (arrow)



Fig. 32.59: Testing extensors of the spine—In the prone position the patient is asked to extend the neck and back against resistance

Muscles of the Upper Limbs (Figs 32.60 to 32.75)



Fig. 32.60: Testing the rhomboids—With the hand placed on the hip, the patient is asked to retract the shoulder while the examiner exerts forward pressure at the elbow. The rhomboids stand up and can be palpitated (see finger)

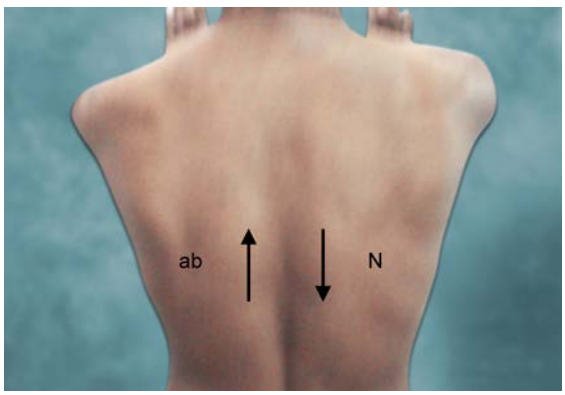


Fig. 32.61: Testing the serratus anterior. The patient pushes against a wall with outstretched arms in front of him. Normally, the medial border of the scapula should remain close to the chest wall (arrows). ab: abnormal; N: Normal



Fig. 32.62: Weakness of serratus anterior—Note the elevation of the scapula from the chest wall (winging) when the patient pushes against the wall without stretched hands (arrow)



Fig. 32.64: Testing the deltoid—The patient is asked to abduct his arm against resistance. The contraction of the deltoid can be seen and palpated. Wasting of the deltoid leads to loss of the rounded appearance of the shoulder (arrow)



Fig. 32.63: Examination of supraspinatus. Contraction of the muscle fibers can be felt during early stages of abduction of shoulder (arrow)



Fig. 32.65: Testing the pectoralis major. Contraction of the muscle can be seen and felt during attempts to adduct the arm against resistance (arrow)



Fig. 32.66: Testing of the latissimus dorsi—On adduction of the horizontally and laterally abducted arm against resistance, the contracting muscle fibers can be seen and palpated



Fig. 32.68: Testing the biceps and brachialis: flexion of the elbow against resistance makes the biceps prominent and its size and consistency can be palpated (arrow)



Fig. 32.67: Testing the infraspinatus—On external rotation of the arm with elbow flexed and kept close to the body, contraction of infraspinatus muscle can be seen and palpated (arrow)



Fig. 32.69: Testing the brachioradialis. On flexion of the semipronated forearm (thumb-up) against resistance, the contracting brachioradialis can be seen and palpated (arrow)



Fig. 32.70: Testing triceps—On attempting to extend the partially flexed forearm against resistance (arrow), contraction of triceps can be seen and palpated



Fig. 32.73: Testing of flexor digitorum profundus. The patient is asked to flex the distal phalanx at interphalangeal joint against resistance after fixing the proximal IPJ (arrow)

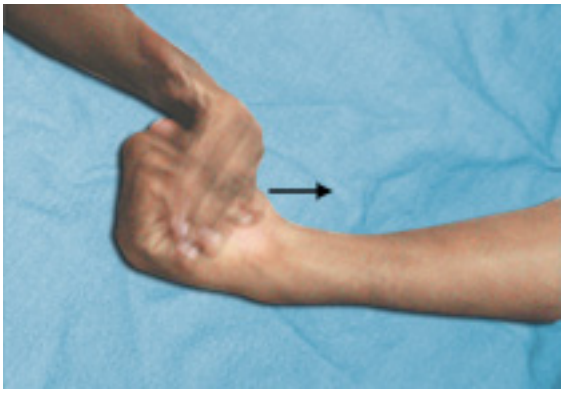


Fig. 32.71: Testing flexors of the wrist—On flexion of the wrist against resistance (arrow), the tendons of flexor carpi radialis and flexor carpi ulnaris can be seen and palpated on the lateral and medial sides of the forearm respectively

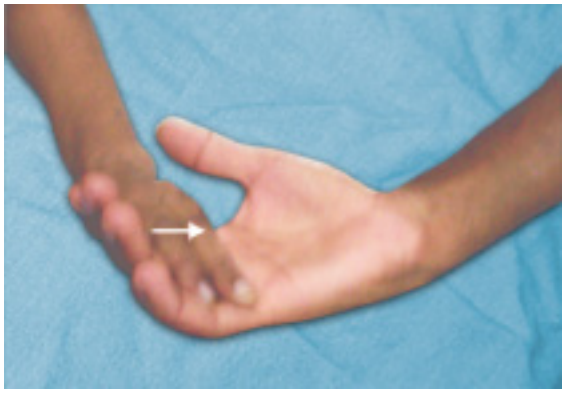


Fig. 32.74: Testing flexor digitorum superficialis—The patient is asked to resists the attempt to straighten the fingers flexed at the PIP joints (arrow). Contraction of the muscle is palpated in the forearm

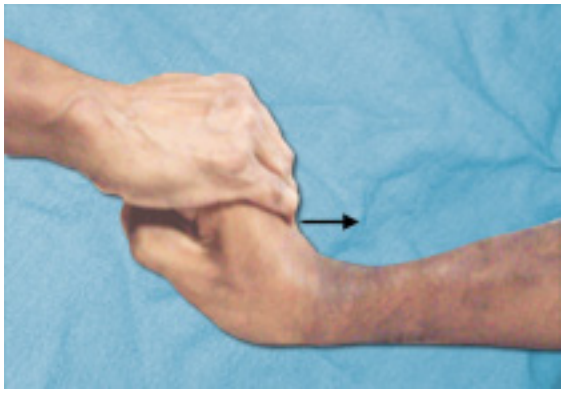


Fig. 32.72: Testing extensors of the wrist—On attempting to extend the wrist against resistance (arrow), the muscle bellies of extensor carpi radialis, extensor carpi ulnaris and extensor digitorum communis can be seen and palpated

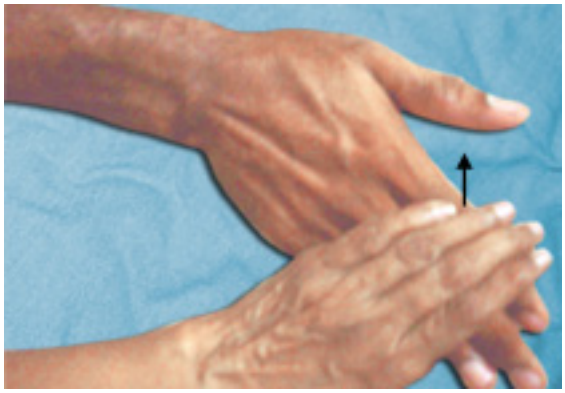


Fig. 32.75: Testing the extensor digitorum communis—With hand outstretched and Interphalangeal joints held in extension,the patient resists the attempt to flex the fingers at the metacarpophalangeal joints (arrow). The contracting muscle can be palpated on the forearm dorsally

Small Muscles of the Hand (Figs 32.76 to 32.80)



Fig. 32.76: Testing of interossei and lumbricals—Ask the patient to hold the fingers straight with flexion at metacarpophalangeal (MCP) joints and extension at interphalangeal joints (IPJ). In paralysis of these muscles, patient is unable to maintain this position. Further testing for resistance to flexion at MCP and resistance to extension at IPJ may be done to confirm weakness

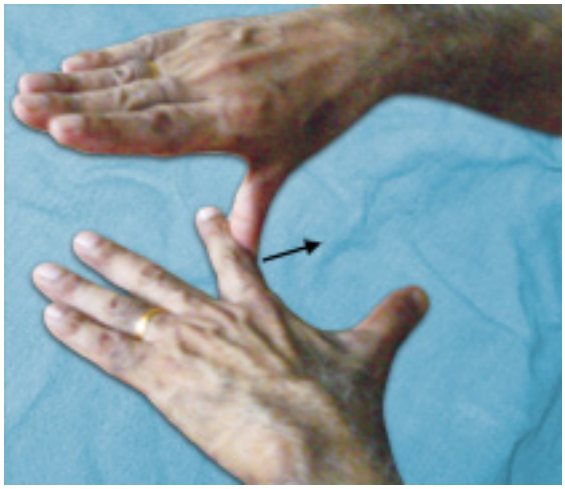


Fig. 32.77: Testing of palmar abductor—First dorsal interosseus—The patient is made to bring the index finger towards thumb against resistance on patient's finger (*see* arrow)



Fig. 32.79: Adduction of thumb—The patient attempts to grasp a paper between the thumb and radial border of index finger. The strength of adductors is assessed by pulling on the paper



Fig. 32.78: Testing of palmar adductors—The patient is asked to hold a paper in between fingers and resist attempts to pull it out (see arrow on the examiner's hand). Compare with the strength of the examiner

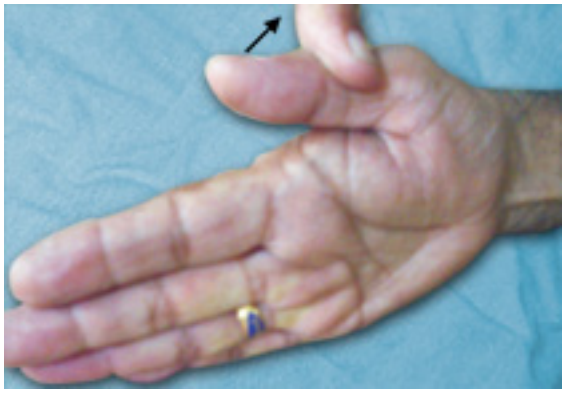


Fig. 32.80: Test for abductor pollicis. The patient attempts against resistance to bring the thumb vertically above its original position (arrow)

Muscles of the Lower Limbs (Figs 32.81 to 32.85)



Fig. 32.81: Testing flexors of the thigh—The patient attempts to flex the thigh against resistance (arrow). The knee is flexed and the leg rests on the examiner's arm

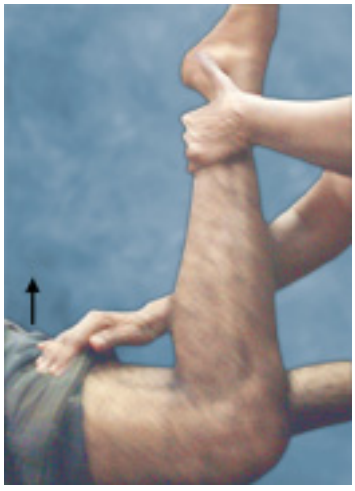


Fig. 32.82: Testing for extensors of the thigh at the hip—The patient lying prone with the leg flexed at the knee attempts to extend the thigh against resistance (arrow). Contraction of the gluteus maximus and other extensors can be seen and palpated



Fig. 32.83: Mild weakness of dorsiflexors of foot is picked-up by asking the patient to stand on heels. Note incomplete dorsiflexion



Fig. 32.84: Mild weakness of plantar flexors can be picked-up by asking patient to stand on toes. Note the weakness of plantar flexion on the right side



Fig. 32.85: Examination of small muscles of foot—Ask the patient to adduct and flex the toes together (cupping). Inability to adopt to this position indicates weakness of the intrinsic muscles. Note individual muscles cannot be tested separately

CHAPTER

33 Special Problems in Neurology

AS Girija, KV Krishna Das

Headache, Coma, Epilepsy, Vertigo-Dizziness-Giddiness complex, Pain, Common pain syndromes

HEADACHE

Headache is one of the common neurological symptoms for which patients seek medical advice. Headache may be acute or chronic. It can vary in severity from a mild ache as is seen in tension headache, to the most excruciating type seen in subarachnoid hemorrhage and meningitis. Severe headache, increased frequency, persistent headache, recent change in the pattern, fear of brain tumor or impending stroke, probably knowledge about a newer modality of treatment or some other similar considerations usually bring the patient to a doctor.

Although the term "headache" can encompass any pain in the head including face, nose, ears, eyes and throat, in common usage, this term refers to pain in the cranial vault. The brain and skull bones *per se* are insensitive to pain. The skin, subcutaneous tissues, muscles, blood vessels and periosteum of the scalp, major dural venous sinuses and their tributaries, portions of the large blood vessels at the base of the brain before they enter the brain substance and the dura mater at the base of the brain are all sensitive to pain. Mechanical irritation, displacement, traction or distension of these structures result in headache. Irritation, stretching and traction on the cranial nerves V, IX and X and upper three cervical roots also can cause headache. Diseases of the pain sensitive structures in the head, such as the eyes, nose and ears give rise to pain which may be referred to the head. Many systemic diseases such as fever, infections, diabetes, hypertension, chronic respiratory failure and others and many drugs can cause or aggravate headache. In the vast majority of patients headache is not associated with any neurological signs. Proper history is the most helpful clinical tool to their diagnosis. In history the following points have to be enquired into:

- Onset and duration
- *Onset:* Acute or chronic duration:
 i. Short duration: lasting hours or days
 ii. Long duration: months or years
- *Paroxysmal or persistent:* If paroxysmal, what is the frequency or periodicity, duration of each attack and precipitating factor?
- *Site:*
 a. Unilateral, bilateral or alternating
 b. Frontal, temporal, parietal or occipital
 c. Direction of spread of headache
 d. Superficial or deep seated pain
- Aggravating and relieving factors
- *Quality of headache:* For example, aching, dull, bursting, throbbing, stabbing, gripping, hitting and others.
- *Severity of headache:* Mild, moderate or severe
- *Associated symptoms:* Visual symptoms, nausea, vomiting, autonomic disturbances, photophobia, irritability.
- Description of a typical attack in case of paroxysmal headache
- *Coughing and others:* Effect of changing the posture of the head, straining at stool, coughing and others.
- Previous treatment and its response

- *Drug intake:* Type of drug, dose and duration.
- Patient's own ideas about his headache and its cause.
- Reason for present consultation.
- Any symptom, referable to the eyes, ears, nose and symptoms suggestive of systemic disorder, e.g. fever, anemia.
- Past history of head trauma and infections of the central nervous system.
- Family history of headache, epilepsy, brain tumor, hypertension, diabetes and mental illnesses, particularly important in chronic cases.
- *Social history:* Patient's way of life, diet, work and attitude to work, hobbies, leisure, family relationships, psychiatric problems. Depending on the duration of illness, headache can be broadly grouped into the following categories.
 - I. Recent headache in an ill patient, e.g. meningitis, brain abscess, brain tumor, raised intracranial tension, acute head trauma, subarachnoid hemorrhage and systemic infections, e.g. typhoid.
 - II. Recent headache in a patient who appears well, e.g. sinus headache, ocular headache, chronic post-traumatic headache, drug induced headache, uncomplicated lumbar puncture headache.
 - III. Longstanding persistent headache, e.g. tension headache.
 - IV. Longstanding, paroxysmal headache, e.g. migraine, sinusitis.

The problem of headache has attracted the attention of neurologists worldwide. The International Headache Society has made a revised classification of headache in 2004. They include:

A. *Primary headache disorder:* Consisting of migraine, tension type headache, cluster-like headache and other trigeminal autonomic cephalalgia and other primary headaches.
B. Secondary heaches dues to other causes.

COMA

Coma irrespective of its cause is a medical emergency, commonly encountered in clinical practice. Most of the cases can be diagnosed by history, physical examination and simple investigations. Coma in many cases is due to metabolic or toxic causes which can be diagnosed and properly managed even in hospitals with only moderate facilities. At least emergency measures should be instituted without delay in every case so as to prevent deterioration and death.

The phenomenon called consciousness has two facets, namely arousal and awareness. These two depend on two brain structures:

i. The brainstem reticular activating system (RAS) which extends from the medulla to the thalamus and
ii. The cerebral cortex. Arousal is the phenomenon of being awake, and it is the primary function of RAS which is a nonspecific transmission system for sensory inputs which activate the cortex. Awareness is a more sophisticated function requiring intact cortical activity in order to interpret the sensory input and respond accordingly. When both arousal and awareness are lost due to dysfunction, either of the cerebral cortex or the brainstem, or both, the patient is said to be in coma. Such a patient does not react spontaneously or to command.

After a quick general examination to assess the vital functions, physical signs that indicate primary CNS pathology or toxic-metabolic etiology should be looked for. Once this differentiation is made, it is comparatively easy to proceed with specific investigations to arrive at the exact dignosis.

Management

Emergency management to save life and to prevent deterioration requires following steps:

Vital Signs

Quickly check the vital signs, i.e.

a. Airway
b. Breathing
c. Circulation.

a. If there is cyanosis or hypoventilation inspect the mouth and throat for foreign bodies and secretions. Remove them and intubate with endotracheal tube and start assisted respiration. If this facility is not available, turn the patient to one side and suck out the secretions in order to establish patency of the airway, or else, allow drainage of secretions by gravity assisted by gentle tapping on the chest with your hands. Try to elicit cough which also helps to dislodge the secretions. Anoxia and airway obstruction can

themselves lead to coma, but more often they aggravate the condition and lead to irreversible brain damage.

b. If coma is due to anoxia, proper ventilation should lead to recovery.

c. In case of cardiac arrest, emergency cardio-respiratory resuscitation should be instituted. Delay beyond three minutes to establish the airways and restore cardiac function can result in permanent brain damage and brain death in patients with cardiac arrest. If the patient is in shock, appropriate corrective measures should be instituted to restore cerebral circulation. If there is any possibility of hypoglycemia rapidly infuse 50 mL of 50% glucose IV. The hypoglycemic patient will rapidly regain consciousness. Even if the patient is in diabetic coma no harm will be done by this glucose administration. Administer 100 mg of thiamine IV simultaneously in order to prevent the development of Wernicke-Korsakoff syndrome.

Drainage

Establish closed bladder drainage using a Foley's catheter and urinary bag. This helps to record the urine volume and to maintain proper fluid output record, apart from preventing wetting of the clothes and the bed.

Consciousness

Determine the level of disturbed consciousness by noting the responses to verbal and painful stimuli.

Drowsy but awakens with stimulation and maintains awareness—Lethargic. Awakens with repeated painful stimulation and awareness is present, though depressed—Stuporous. Awake but not aware—Vegetative state. Neither awake nor aware—Comatose-Glasgow coma scale may be used to assess the depth of coma especially due to head trauma (see Chapter 32).

History

If history can be obtained from any source, enquire into the following:

a. *Mode of onset of coma:*

• Instantaneous	Cardiac arrest, subarachnoid hemorrhage, pontine hemorrhage, basilar artery occlusion, epilepsy, head trauma.
• Within minutes	Head trauma, intracranial hemorrhage, cerebral infarction, brain herniation due to intracranial space occupying lesions, epileptic or non-epileptic convulsions, status epilepticus, Stokes-Adam's attacks, psychogenic cause (hysteria).
• Minutes to hours	Hypertensive encephalopathy, hypotension, hypoglycemia, fluid and electrolyte disturbances, fulminant in-fections of the CNS, over-dosage of sedative drugs.
• Hours to days	Respiratory insufficiency, diabetic coma, uremic coma, hepatic failure.
• Fluctuating coma	Subdural hematoma, fluid and electrolyte disturbances.
• Bizarre behavior	Psychogenic.

b. *Past history:* Past history of recurrent coma, headache, vomiting, convulsions, vertigo, dysarthria, dysphagia, dysphasia and focal sensorimotor symptoms to indicate any CNS lesions. Details of medication and history of discontinuation of medication should be enquired into. History of diabetes, hypertension, epilepsy and others and occurrence of recent head trauma may give clue to the underlying cause.

c. *Habits and addictions:* Use of alcohol and other narcotic substances.

d. *Psychiatric history*: Ascertain psychiatric history, especially for catatonic stupor and hysteria.

e. *Other factors:* Circumstances under which the comatose patient was first seen.

Physical Examination

The objectives of physical examination are:

i. To differentiate coma due to an organic cause from "coma" of psychogenic orgin

ii. To differentiate coma due to a CNS lesion from metabolic or toxic coma and

iii. To establish the pathological lesion.

The procedure for examination is given below:

a. General examination: After performing a routine general examination particularly look for the physical signs given in Table 33.l.

b. Neurological examination: Particularly look for abnormalities of pupils, eye movements including reflex movements such as oculocephalic and oculovestibular reflexes, pattern of breathing, motor response and signs of meningeal irritation (Tables 33.2 to 33.4).
c. Examination of the other systems—Cardiovascular, respiratory, alimentary, excretory, endocrine and others should be examined. Particularly look for overt or occult trauma over the head or other parts of the body. Carefully look for evidences of poisoning, either ingested or self-injected.

Abnormal Breathing Patterns in CNS Disorders

Cheyne stokes respiration	Periodic breathing in which respiratory cycles gradually wax and wane, i.e. hyperpnea alternate with cycles of apnea.
Central neurogenic hyperventilation	Continuous, regular, rapid, deep respiration.

Table 33.1: General physical examination—diagnostic clues for coma

Examination	*Findings*	*Possibilities*
Skin and mucous membranes	Evidence of trauma	Cerebral contusion, extradural or subdural hematoma.
	Needle prick marks	Drug addiction
	Hemorrhages	Bleeding disorders, anticoagulant overdose leading to cerebral hemorrhage
	Maculo-hemorrhagic rashes	Meningococcal infection, staphylococcal endocarditis
	Hemorrhagic blisters	Barbiturate coma
	Spider naevi, jaundice	Hepatic coma
	Cyanosis	Inadequate oxygenation, anoxia and carbon dioxide narcosis, carbon monoxide poisoning.
	Marked pallor	Internal bleeding and shock, neuroleukemia
	Excessive sweating	Hypoglycemic coma, shock
Temperature	Moderate or high fever (up to 41)	Systemic or CNS infection, brainstem hemorrhage
	Temperature, above 42°C	Heat stroke.
	Temperature below 35°C	Myxedema coma, barbiturate coma, alcohol intoxication, exposure to cold
Pulse	Bradycardia (less than 60/mt)	Raised intracranial pressure, myxedema coma, heart block
	Tachycardia (more than 100/mt)	Systemic infections, cardiac arrhythmias
	Arrhythmias	Embolism due to atrial fibrillation, Stokes-Adam's attack in heart block
Blood pressure	High	Hypertensive encephalopathy, raised intracranial pressure cerebrovascular accidents (reactive hypertension)
	Low	Shock, internal bleeding, myocardial infarction, diabetic coma, gram-negative septicemia, intoxication, barbiturate coma
Odor of the breath	Fruity odor of acetone	Diabetic coma, ketoacidosis
	Other odors	Uremic coma, hepatic coma, others metobolic comas poisoning
Respiration	Shallow	Narcotic overdose, raised intracranial pressure
	Deep and rapid	Pneumonia, diabetic coma, uremic coma, central neurogenic hyperventilation
	Cheyne-Stokes respiration	Raised intracranial pressure brainstem lesion, metabolic coma
Pupils	Normal in size, equal, reacting to light	Metabolic coma
	Asymmetrical in size and light reaction	Focal CNS lesions

Table 33.2: Differentiating features of coma due to CNS lesions and toxic-metabolic coma

	Coma due to CNS lesion		*Toxic-metabolic coma*	
Clinical features	*Common finding*	*Exception*	*Common finding*	*Exception*
Respiration	Irregular	Regular in central neurogenic hyperventilation	Regular	Cheyne-Stokes respiration in pulmonary insufficiency, apneic breathing in narcotic overdosage
Pupils Size and symmetry	Asymmetrical	Symmetrical and constricted in midbrain and pontine lesions. In the later stages both pupils are dilated and fixed	Symmetrical, normal size	Symmetrical dilatation in atropine and glutethemide poisoning and anoxia. Symmetrical constriction in morphine poisoning. Asymmetry due to pre-existing eye disease
Reaction to light	Sluggish or absent	Normal in diffuse CNS infection	Normal except in the terminal stages	Absent in atropine and glutethemide poisoning
Oculocephalic and oculovestibular reflexes	Absent or asymmetrical	–	Present	Absent in barbiturate and diphenylhydantoin intoxication
Unilateral decorticate or decerebrate posture	Present	May be bilateral in rostrocaudal herniation	Absent	May be present bilaterally
Optic fundi	Papilledema if intracranial pressure is elevated	–	No papilledema	Papilledema, if cerebral edema is severe.
Muscle stretch reflexes	Asymmetrical	Symmetrical in rostrocaudal herniation, pontine hemorrhage, diffuse CNS infections	Symmetrical	Asymmetrical due to pre-existing neurological condition
Neck stiffness	Present in subarachnoid hemorrhage, meningitis, tonsillar herniation	As coma deepens, neck stiffness may disappear	Absent	Sometimes meningism may be present in uremia
Myoclonus	Absent	Unifocal or symmetrical in slow viral diseases of CNS	Absent	Multifocal myoclonus may occur uncommonly
Focal neurological deficit.	Present	Absent in diffuse CNS infections.	Absent	If present, it may be a pre-existing neurological disease
Convulsions	Focal or focal becoming generalized	Generalized in diffuse CNS infections	Generalized	Focal if there is associated cerebrovascular disease
Progression of unconsciousness through the stages of delirium, confusion, stupor and coma	Does not occur	May be present in diffuse CNS infections	Present	–

Note: In hysterical coma: none of the abnormalities described in organic brain disease will be present. The behavior of the patient will be abnormal. When the eyelids are passively opened, the eyeballs usually roll up. Plantar response will be bilaterally flexor.

Apneustic respiration	Regular breathing with longer pauses for 2 to 3 seconds after each inspiration.
Ataxic respiration	It is a chaotic breathing in which the rate, rhythm and depth of respiration are all irregular.
Hypoventilation	Regular, rhythmic, shallow breathing.

How to Recognize Paralysis in a Comatose Patient?

Presence of any or all of the features given below should suggest paralysis:

1. Lack of spontaneous movements of the limbs on one side.
2. Lack of withdrawal in response to painful stimuli on one side.
3. Tendency for the limb to remain in any position even if it is an uncomfortable one.
4. Externally rotated position of one lower limb.
5. The thigh on the paralyzed side appears to be wider and flatter than the other.
6. When the limbs are lifted above the bed and allowed to drop down, the paralyzed limb falls flaccidly.

Table 33.3: Site of lesion and the clinical features

Site of lesion	*Pupils*	*Eye movements*	*Respiration*	*Motor behavior*
Cerebral hemisphere	Normal and reactive, or dilated and fixed pupil ipsilaterally due to uncal herniation	Conjugate deviation of eyes away from the side of paralysis, i.e. looks towards the lesion. Tonic conjugate deviation to cold caloric test	Cheyne-stokes respiration (CSR)	Hemiplegia or decorticate posture contralateral to lesion
Diencephalon	Ipsilateral, small reactive pupil in anterior lesion, normal size, nonreactive pupil in posterior lesion. Unilateral hippus	Conjugate deviation of eyes opposite to the side of lesion in unilateral thalamic lesions, both eyes deviate down and inwards in midline lesions. Tonic conjugate deviation to cold caloric test	Normal or CSR	Decorticate posture contralateral to lesion
Midbrain	Bilaterally symmetrical and fixed in mid-position	Downward and inward deviation of both eyes, cold caloric and oculocephalic reflexes absent. Retraction convergence nystagmus	CSR or central neurogenic hyperven tilation	Decorticate or decerebrate posture, contralateral to lesion
Pons	Bilaterally symmetrical and fixed in constricted position (pin-point pupils)	Same as for midbrain lesion except that instead of nystagmus, ocular bobbing may be present and there may be conjugate deviation of eyes towards the paralyzed side (looks away from lesion). (Bobbing means moving up and down in a jerky manner)	Apneustic or cluster respiration.	Extension of arms with flexion of legs, or decerebrate posture
Medulla Consciousness is not lost unless there is rostrocaudal herniation or brainstem compression	Normal	Normal	Ataxic	Flaccid limbs

Note: If the coma is due to primary CNS disease, the next step is to localize the lesion in the nervous system. Observation of the pupils, ocular movements including reflex movements, patterns of respiration and motor behavior help to localize the site of pathology in the brain, as shown in the Table 33.3

Table 33.4: Summary of clinical features which suggest etiopathogenesis of coma

Clinical features	*Etiology*
1. Coma with focal neurological signs	CNS diseases, e.g brain tumor, abscess, hemorrhage, infarction, hypertensive encephalopathy, subdural hematoma, cerebral contusion, encephalitis
2. Coma without focal neurological signs, but with signs of meningeal irriation	Meningitis or subarachnoid hemorrhage
3. Coma without focal neurological signs or signs of meningeal irritation	Metabolic or toxic coma: alcohol intoxication, barbiturate overdose, hepatic coma, diabetic coma, hypoglycemia, uremia, fluid and electrolyte disturbance, myxedema coma, other poisons

7. If there is facial palsy, the cheek on the paralyzed side puffs out with each expiration. Remember the following:

i. *All that glitters is not gold:* It is a well known saying. It also applies to a comatose patient. For example, alcoholic odor in the breath of a comatose patient does not necessarily indicate that alcoholic intoxication is the only cause of coma in him. It could as well be due to head trauma or poisoning sustained under the influence of alcohol.

ii. *Which came first, hen or egg?:* It is another universal unsolved dilemma. Such a dilemma often arises when one is dealing with a comatose patient. For instance whenever, a

person falls down especially from a height and is found in an unconscious state, there could be at least two possibilities. One possibility is that the fall could have resulted from a stroke and the injuries are secondary to fall or alternatively, he might have fallen down and sustained head injury that led to unconsciousness and hemiplegia.

iii. *Beware of the red herring:* Presence of an obvious cause for coma in an individual should not make the physician blind to other possibilities. For example, an elderly diabetic with painful polyneuropathy may become comatose, not due to his diabetic state but it may be due to overdose of sleeping pills he had consumed the previous night to get over his painful peripheral neuropathy.

iv. *Guard yourself:* In these days of increasing suicidal and homicidal tendencies, consider the possibility of sedative drug overdose and blunt head injury in all those patients in whom no other cause for coma is obvious and where the circumstances are suspicious. Do not forget to collect the gastric contents and blood samples for drug assay and inform the appropriate legal authorities if unnatural circumstances are suspected.

v. *Act fast:* Almost all cases of metabolic-toxic coma and many cases with CNS lesions are potentially reversible conditions, provided they are managed promptly and properly. Delay and mismanagement make a reversible condition irreversible. At that stage any action will be too late to be beneficial. So, you should act fast.

EPILEPSY

The term "seizure" can be applied to describe any or all the clinical manifestations of epilepsy. However, when these manifestations occur as isolated episode or they are manifestations of some other acute illness such as encephalitis or a toxic-metabolic disorder, they are called seizures and not epilepsy. By definition, epilepsy is a recurrent disorder occurring in an otherwise healthy person over a period of time. Therefore, it will be more appropriate to state that all patients who have seizures may not be suffering from epilepsy but every one who has epilepsy has seizures. The term "convulsion" is applied to describe any of the motor manifestations of a seizure. "Fit" is a layman's term for seizure.

Originally, epilepsy was classified into grand mal, petit mal, Jacksonian and psychomotor (temporal lobe) types. Based on clinical, electro-encephalographic (EEG), neuradiological and/or pathological correlations, a new classification of epileptic seizures has been put forward, which is widely accepted. This is known as the "International Classification of Epileptic Seizures". However, only after a thorough clinical and investigative work up it is possible to determine accurately the type of epilepsy according to this International classification. As it is not always possible or practicable to get access to all these investigative facilities in many parts of India, only the clinical pattern of seizure disorders conforming to the International classification, will be described below.

Based on clinical symptomatology, epileptic seizures can be broadly divided into two types:

1. Generalized seizures
2. Partial seizures.

1. *Generalized seizures* are bilaterally symmetrical seizures and do not have a focal onset (primary generalized seizures). They can be further subdivided into seven types:
 i. Generalized tonic-clonic seizures or grand mal seizures
 ii. Generalized tonic seizures
 iii. Generalized clonic seizures
 iv. Bilateral myoclonic seizures
 v. Absence seizures—typical petit mal and atypical forms.
 vi. Atonic seizures
 vii. Infantile spasms.
2. *Partial seizures* are characterized by initial symptoms localized to one region of the body depending on the site of seizure focus in the brain. They can be further subdivided into the following three types:
 i. Simple partial motor seizures, including Jacksonian seizures
 ii. Simple partial sensory seizures
 iii. Complex partial seizures (psychomotor or temporal lobe seizures).

In simple partial seizures, consciousness is not altered whereas complex partial seizures may be associated with alteration in consciousness.

Partial seizures may progress into generalized tonic-clonic seizures. Sometimes, the secondary generalization occurs so fast that the initial focal onset may be missed clinically. EEG may be required to reveal its focal nature.

Unilateral seizures are seizures strictly confined to one side of the body. Unclassified seizures are those to which accurate label cannot be given due to inadequate or incomplete information regarding the seizure pattern.

Usually primary generalized seizures have their onset in the first or second decade of life, they are not associated with mental retardation or focal neurological signs and they have a strong familial tendency. As opposed to this, partial and secondary generalized seizures may start at any age, fequently they are associated with focal neurological signs or papilledema and there is no familial tendency.

Etiologically, epileptic seizures can be classified as:

i. Idiopathic, in which the brain is macroscopically and microscopically normal
ii. Symptomatic, in which a definite cerebral lesion is demonstrable.

Primary generalized seizures are usually idiopathic. Partial seizures are almost always caused by focal lesions such as craniocerebral trauma, intracranial tumor, brain abscess, cerebrovascular accidents, glial scars and others. In metabolic, hypoxic and toxic encephalopathies and some primary diseases of the brain such as bacterial meningitis, viral encephalitis, subacute sclerosing panencephalitis (SSPE), Creutzfeldt-Jakob disease and lipid storage disorders, there may be generalized convulsive seizures.

In the work up of a patient with seizures, clinical history is most important for initial classification of the seizure type. Complete physical and neurological examinations is necessary to determine the underlying cause.

Generalized tonic-clonic seizure (grand mal type): A generalized convulsion passes through three phases—tonic, clonic and postictal phases. The tonic phase starts without any warning symptoms. The arms go into abduction, elbows flex and hands pronate. The mouth opens widely, so also the eyes. Soon the patient loses consciousness and falls to the ground abruptly. This is followed by clenching of the jaws, often with biting of the tongue. A loud cry may occur when air passes through the partially closed vocal cords—epileptic cry. All muscles go into tonic spasm. Respiration stops for a while and the patient becomes cyanosed. The pupils become dilated and nonreactive. This tonic phase lasts for about 10 to 15 seconds, and gradually the clonic phase begins.

It starts as a mild, generalized trembling, rapidly going on to rhythmic, symmetric, intermittent muscular contractions called clonic jerks. The eyeballs roll up. Excessive salivation and frothing from the mouth develop. There will be excessive sweating. Micturition, defecation or seminal ejaculation may occur. The entire clonic phase lasts for 1 to 2 minutes during which period the breathing is irregular.

At the end of the clonic phase, the patient takes a deep inspiration and lies still in deep coma for a variable period lasting from a few minutes to several hours. When he wakes up he is disoriented and confused (postictal state). He may sleep for several hours and wake up with headache and bodyaches. In most cases the incident is not remembered. Injuries resulting from the fall and violent convulsions and biting of the tongue are common. This type of convulsions may occur singly or in clusters, either during wakefulness or during sleep. Majority have their age of onset in the first or second decade. Usually there will be positive family history of epilepsy. During the interictal period neurological examination reveals no abnormality.

Aura: It is a symptom or symptom complex which the patient experiences just before a seizure and regards it as a sign of an impending seizure but actually, the aura is the initial event of the seizure itself. The aura may be in the form of palpitation, a sort of sinking, or gripping feeling in the abdomen, or gas rising up in the epigastrium, or some other undesirable sensation in some part of the body. The patient should be asked about the aura because it may give a clue to the site of the seizure focus. Approximately half the cases of generalized convulsive seizures experience some type of aura.

Tonic seizure: It is characterized by the development of sudden opisthotonus posture with loss of consciousness and marked autonomic manifestions such as sweating and alteration in pulse rate, respiration and blood pressure.

Clonic seizure: It is characterized by sudden, bilateral, rhythmic clonic movements of the limbs,

with or without loss of consciousness and autonomic manifestations as in tonic seizures.

Myoclonic seizures: It is characterized by sudden, bilaterally symmetrical, isolated jerking of the limbs.

Infantile spasms (syn: hypsarrhythmia: salaam spasms): These occur in infants between the age of 3 to 12 months. Each attack is characterized by sudden forward bending of the trunk and head with extension of the arms and legs. They occur several times in a day. The child may be otherwise normal or show developmental arrest and mental retardation.

Atonic seizures: These are characterized by sudden loss of postural tone with sagging of the head and falling to the ground, without losing consciousness (drop attacks), usually occurring in children.

Absence seizures: These are characterized by sudden cessation of all activities, loss of responsiveness and a staring look, lasting for about 3 to 30 seconds. Usual age of onset is 3 to 13 years. These spells may or may not be associated with minor motor activities in the form of chewing, smacking movements of the lips, fluttering of eyelids, or rolling up of the eyeballs. Usually the patient is not aware of these episodes. They are recognized by others as brief pauses during conversation, eating, writing, reading or any other motor activity.

Typical absence attacks can be precipitated by hyprventilation for about 3 minutes. Unlike a grand mal seizure, there is no postictal confusion, drowsiness or headache. The attacks may occur several times in a day. Atypical absence attacks have slower onset, longer duration and gradual cessation. They may be associated with more complex motor activities and automatism.

Partial Motor Seizures

These are characterized by turning of the head and the eyes to one side with tonic contractions of an extremity and trunk, without loss of consciousness (adversive seizures). At times there may be tonic or clonic movements in one part of the body, usually at the angle of the mouth, thumb or the foot because these areas have greater cortical representation. These attacks usually last for 20 to 30 seconds. When the attack begins at one of these areas and progressively marches to involve contiguous anatomical parts of the body, it is called Jacksonian seizure. There may be postictal focal paralysis (Todd's palsy) which may last for a few hours or even up to 3 to 4 weeks.

Partial Sensory Seizures

Somatic sensory seizures are characterized by recurrent transient attacks of "pins and needles" sensation, numbness and rarely pain or thermal sensation over one part of the body. Special sensory seizures are characterized by recurrent, transient attacks of special sensory phenomena the nature of which depends on the site of lesion in the brain (Table 33.5).

Complex Partial Seizures

These are characterized by formed hallucinations, illusions, dyscognitive experiences such as deja vu (a feeling of intense familiarity), dreamy state, depersonalization and others. Affective states such as fear, depression or elation, and automatisms may occur. These are caused by a focus usually in the temporal lobe, but sometimes in the frontal lobe as well.

Status Epilepticus

Status epilepticus is defined as "an epileptic seizure which is so prolonged or so frequently repeated as to create a fixed and lasting epileptic condition". In other words, a seizure which is very prolonged or which recurs at brief intervals can be called status epilepticus. Any type of seizure may go into status epilepticus although generalized tonic-clonic

Table 33.5: Clinical manifestation of seizures for corresponding sites of lesions

Site of lesion	*Clinical manifestation of seizure*
1. Lateral surface of occipital lobe	Visual phenomena in the form of darkness or spots of light which may be static or moving
2. Posterior part of occipital lobe	Complex visual hallucinations
3. Posterior part of temporal lobe	Rarely auditory hallucinations
4. Posterior part of superior temporal gyrus	Vertigenous sensation
5. Inferior and medial parts of temporal lobe (uncus and hippocampus)	Olfactory hallucinations
6. Temporal lobe	Gustatory hallucinations
7. Insulo-orbital cortex or cingulate cortex	Visceral sensations arising from the thorax, epigastrium and the abdomen

convulsive status is more frequent, more serious and easily recognisable.

Status epilepticus may be of the following types:

i. Generalized convulsive type
ii. Partial convulsive type, i.e. epilepsia partialis continua, or
iii. Nonconvulsive type, i.e. absence status.

In generalized convulsive status, generalized convulsions follow each other so closely that consciousness is not regained in between the attacks, or more than three convulsions occur within 30 minutes or single convulsion lasts for more than 10 minutes.

In *epilepsia partialis continua,* focal motor convulsions persist nonstop for hours, day or even months.

Absence status is difficult to recognise as it presents like a "dreamy" state or "twilight" state or unresponsive state. Status epilepticus may occur *de novo* in a previously healthy individual during acute illnesses such as encephalitis, meningitis, head trauma, cerebral anoxia, stroke, tumors of the frontal lobe and metabolic disturbances. More commonly it occurs in persons who are known to have epilepsy, especially if they have stopped the anticonvulsant drugs prematurely and abruptly. Status epilepticus is a medical emergency and if not managed promptly and properly will lead to morbidity and mortality.

Special Types of Seizure Disorders

Neonatal Seizures

Unlike grown up children, neonates do not manifest typical features of epilepsy. The seizures in this age group may be in the form of brief episodes of eye deviation to one side, frequent blinking, repetitive sucking movements, pedalling movements of the legs, apneic spells, tonic extension of all the extremities and focal or multifocal myoclonic jerks. The common causes are hypoxic-ischemic brain damage, intracranial hemorrhage, meningitis, inborn errors of metabolism, pyridoxine deficiency, hypocalcemia and hypoglycemia.

Febrile Convulsions

This is the most common type of seizures in infants and children in the age group from 6 months to 5 years. Brief, generalized tonic-clonic convulsions occur in association with fevers. The fever may be mild or moderate. This may follow or precede the convulsion. Neurological examination will be normal in between the attacks.

Sometimes, there may be family history of febrile convulsions or epilepsy. These type of seizures are called simple febrile convulsions.

A febrile convulsion is termed "complicated febrile convulsion" under the following circumstances:

i. when a convulsion lasts for more than 15 minutes;
ii. when convulsions occur in quick succession;
iii. when a convulsion is focal or focal becoming generalized or
iv. when there are associated neurological or EEG abnormalities.

In all such cases, examination of the cerebrospinal fluid is mandatory to exclude infection of the CNS. Children with recurrent febrile convulsions require full neurological investigation and prolonged anticonvulsant medication.

Benign Rolandic Epilepsy

It is a focal or partial seizure disorder, but without any demonstrable focal pathology in the brain. Usually, it occurs in children of school going age and spontaneously ceases during adolescence. It is important to recognise this disorder because it has excellent prognosis in spite of its focal nature. Typically it is characterized by generalized convulsions that occur in sleep or soon after waking up in the morning. Convulsions are usually preceded by orofacial paresthesia, facial twitchings and difficulty in speech. The characteristic findings on the EEG include spikes or sharp waves confined to the rolandic area.

Late Onset Epilepsy

Seizures occurring for the first time after the age of 30 years are referred to as late onset epilepsy. Usually, these are either partial seizures or partial becoming secondarily generalized. They have to be considered as symptomatic seizures unless proved otherwise. Acute causes include CNS infections, metabolic or hypoxic encephalopathies and intracranial vascular occlusion or hemorrhage. Common chronic causes include slow-growing brain tumors, old infarcts, glial scars following head trauma, cerebral tuberculomas and cysticercosis.

Clinical Approach to a Case of Epilepsy

1. Consider epilepsy in every patient who presents with sudden, transient and recurrent attacks of symptoms suggestive of CNS dysfunction.
2. Obtain a detailed history from the patient and at least from one eye witness to these episodes.
3. Inquire into the following:
 - Age of onset of symptoms.
 - Accurate and full description of one attack if the attacks are stereotyped. Otherwise description of each type of attack separately.
 - Particularly inquire about aura, focal onset of a convulsion, loss of consciousness, tongue bite, frothing from the mouth, bladder or bowel incontinence, sustained injuries, postictal phenomena, interictal symptoms and frequency of the attacks.
 - Epileptic attacks are precipitated by several stimuli. In many cases attacks are precipitated by avoidance of the drug, failure, travel, insomnia, photic stimulation by cinema or television, late dinner and others.
 - Past history of trauma, CNS infections, febrile convulsions or any other neurological disorder should be elicited.
 - Medication history, with details of antiepileptic drugs and their dosage. If drug has been discontinued, reason for doing so.
 - After taking the history, perform full general examination and detailed neurological examination.

Having done all this, decide whether the patient is having seizures or not. ***Epilepsy has to be differentiated from conditions such as syncope, Stokes-Adam's attacks, hypoglycemia, tetany and hysterical fits.*** If it is seizure, determine its type and possible cause. Plan for full investigation in all cases. The advent of CT scan and MRI has revealed underlying causes such as slow growing tumors, cysticercosis, tuberculoma and others in patients thought to be having idiopathic epilepsy. After confirming the diagnosis, start therapy with the appropriate anticonvulsant drug in adequate dosage.

VERTIGO-DIZZINESS-GIDDINESS COMPLEX

Dizziness or giddiness is yet another common symptom, for which many seek medical advice. Although in most of these patients, the condition may be benign, the symptom is most alarming to the patient. Basically, all these patients have a feeling of disequilibrium in space. Normal spatial equilibrium is a multimodal function dependent on the integration of vestibular, visual, proprioceptive and cerebellar inputs to the brain. It may be disturbed either primarily or secondarily, due to a variety of causes. Several terms may be used by patients to describe their feeling of disequilibrium. These include dizziness, giddiness, whirling, rotation, spinning, light headedness, shaking, swaying, wobbling, instability, unsteadiness, vertigo and probably others too.

The most useful clinical subdivision is to categorize these symptoms into:

i. True vertigo and
ii. Pseudovertigo.

True vertigo denotes a sense of rotation in one direction, which may be "subjective", when the subject feels he is rotating in his environment or "objective" when he feels the objects in his environment are rotating around him. Pseudovertigo, which is much more common than true vertigo, encompasses all sensations of disequilibrium, other than true vertigo. True vertigo is due to primary neurological causes such as dysfunction of vestibular end organ (labyrinth), vestibular division of eighth cranial nerve, vestibular nuclei in the brainstem and their connections, flocculonodular lobe of the cerebellum and very rarely cerebral hemisphere. Often pseudovertigo may be due to non-neurological causes. In true vertigo, in addition to feeling of rotation, other symptoms may coexist. These include impulsion, i.e. a feeling of being pulled to the ground or to one side; tinnitus, deafness, diplopia or other focal neurological deficits. True vertigo occurs as a single episode or recurrent stereotyped attacks of definite duration. Pseudovertigo occurs either as momentary attacks or as a very prolonged sensation lasting for hours or even days.

When confronted with a patient having vertigo or dizziness or some other similar complaint, enquire into the following:

1. Is it a true vertigo or pseudovertigo?
2. Is it paroxysmal or persistent?
3. Is it associated with symptoms like nausea, vomiting, tinnitus, deafness, diplopia or any other symptom?

4. *Positional factors:* Whether vertigo occurs during head movements or only in certain positions of the head or during change of posture, etc.
5. *Precipitating factors:* For example, exercise, food intake, salt intake, stress and others.
6. *Exacerbating factors:* For example, noise, straining, coughing, exercise and others.
7. *Alleviating factors:* Change of head position or body posture.
8. *Drug history:* For example, aminoglycoside antibiotics, anticonvulsants especially diphenylhydantoin, antihypertensive drugs, salicylates, etc.
9. *Past medial history:* Head injury, ear infection or trauma, antecedent upper respiratory infection, diabetes, psychiatric illness, and others.
10. *Family history:* Particularly for familial deafness, intracranial tumors and neurofibromatosis.

During physical examination carefully elicit the following:

1. Hearing deficit
2. Nystagmus and its type
3. Ocular movements and visual acuity
4. Cerebellar signs
5. Sensory deficits, especially prorioception
6. Neck movements for evidence of cervical spondylosis, precipitation of vertigo in a particular position of the head, presence of vascular bruit in the neck.
7. Cardiovascular evaluation: Peripheral pulses, pulse rate and rhythm, blood pressure in supine and erect postures.
8. Reproduction of the symptom on hyperventilation.

Patient with this symptom complex may fall into any one of the following categories:

1. Paroxysmal attacks of momentary nature
2. Paroxysmal attacks of longer duration
3. Persistent symptoms with no neurological signs
4. Persistent symptoms with neurological signs
5. Single, severe attack.

PAIN

General Considerations

Pain is body's most important alarm system because it draws attention to the fact that something is at fault and compels the patient to seek medical help. Total absence of pain sensation is as disastrous as uncontrolled severe pain. Both can do serious harm to the body and the mind. However, uncontrolled pain is the single most common reason for people to seek medical advice.

Pain signals received from sense organs enter the spinal cord through the posterior nerve roots. In the spinal cord, pain conveying fibers occupy two distinct pathways, i.e. the lateral and medial systems. The lateral system conducts impulses rapidly and it is concerned with the transmission of sudden phasic pain to the cerebral cortex. The topographic arrangement of its fibers helps to localize sudden sharp pain and also to appreciate different qualities of pain such as burning, pricking, throbbing and others. The medial system differs from the lateral system in many ways. It is responsible for diffuse, unpleasant, persistent sensation of pain. The pain is felt sometime after an injury because the fibres conduct the impulses relatively slowly. The medial system also influences the emotional components of pain, through its connection with the limbic system of the brain.

The activity in the lateral system that gives rise to sudden phasic pain is quickly inhibited by a system of neurons that arise in the periaqueductal gray matter in the midbrain and descends downward to the dorsal horns of the spinal cord, where it inhibits transmission of pain signals from the peripheral nerves to the ascending tracts. This descending inhibitory system can be activated by endogenous opioid substances such as endorphins and enkephalins. It is not clear whether pain appreciation takes place in the sensory cortex but corticofugal fibres inhibit afferent transmission of pain conveying fibers. Since the pathways conducting pain are distinct, various ablative surgical procedures came into vogue to relieve intractable pain.

The "Gate Control Theory of Pain" and its Practical Implications

The "gate control theory of pain" was proposed in 1965. According to this theory, only a limited number of sensory impulses can be processed by the nervous system at any given moment. When too many impulses impinge upon the spinal cord from the periphery, certain cells in the dorsal horn of the cord interrupt these impulses from entering the tracts as if closing an entry gate. Thus, the pain sensation

which is transmitted by C fibers at a slow rate can be prevented from entering through the "gate" into the cord, when there is a competition from other non-pain sensory impulses, conveyed by faster conducting nerve fibers. Small neurons in the substantia gelatinosa of the posterior horn of the spinal cord are also able to prevent pain impulses coming through the dorsal roots. It is also possible that descending fibers from the brainstem, thalamus, limbic system and other areas in the brain also control the gate mechanism in the spinal cord.

COMMON PAIN SYNDROMES

Pain Occurring in the Region of the Face and Throat

Several types of pain occur in face, throat and neck and many of them have characteristic diagnostic features. A proper understanding of the various clinical entities is necessary for an accurate diagnosis and management. The diagnosis mainly rests on the history and therefore a detailed history is important.

Trigeminal neuralgia (Tic douloureux): It is a recurrent, paroxysmal, brief episode of intense pain over one side of the face. The pain may be described as lancinating, lightning-like, shooting or electrical shock-like sensation. The pain is usually confined to one of the three divisions of the trigeminal nerve, maxillary division being the most commonly affected one and the ophthalmic division least affected. Paroxysms may last only for a few seconds or up to several minutes. Their frequency varies from once in a few minutes to only once or twice a day. Trigger zones may be present. Trigeminal neuralgia may be idiopathic or secondary.

Glossopharyngeal neuralgia: Although it is less common, it resembles trigeminal neuralgia in many respects. It is also a recurrent, paroxysmal, intense pain that originates in the tonsillar fossa and may radiate to the ipsilateral ear. Sometimes, the vagus nerve may also be involved in which case the pain may be accompanied by bradycardia and even syncope. Swallowing, talking, chewing, yawning, laughing or similar acts trigger the pain. There will be no demonstrable evidence of sensory, motor or reflex deficits of IX and X cranial nerves. Rarely, glossopharyngeal neuralgia may be secondary to peritonsillar abscess or carcinoma of the oropharynx.

Occipital neuralgia

Paroxysmal pain in the occipital, suboccipital and posterior parietal areas on one side may occur due to spontaneous irritation of the greater occipital nerve. Sometimes, the pain in this distribution may be provoked by touching the skin in that area.

Temporomandibular neuralgia (Costen's syndrome): This condition, seen in the young or elderly individuals is characterized by recurrent, unilateral, severe pain that originates in one temporo-mandibular joint and spreads either into the face or into the temporalis muscle. The pain is provoked by the movements of the lower jaw during chewing, yawning and talking. These movements may be associated with clicking sound in the temporomandibular joint. The temporomandibular joint and temporalis muscle are usually tender on palpation.

Postherpetic neuralgia: Ophthalmic herpes: In the elderly patient, herpes zoster ophthalmicus may lead to the development of neuralgic pain in the distribution of ophthalmic division of the trigeminal nerve. The discomfort of the acute stage will be followed by chronic, intractable, constant, burning sensation with superimposed episodes of stabbing pain. Even slight touch on the affected skin provokes intense pain.

Intermittent claudication of the masseters: Sometimes in temporal arteritis, the arteries to the muscles of mastication and tongue may be involved. Such patients have pain in the masseter and tongue muscles on chewing movements due to intermittent claudication of these muscles.

Paroxysmal Hemicranial Cephalalgia

This is characterised by paroxysmal, throbbing, unilateral, headache and facial pain, accompanied by mydriasis and perspiration on the affected side. In between the attacks of headache, there will be ipsilateral Horner's syndrome. There will be past history of trauma to the anterior triangle of the neck, probably affecting the carotid artery sheath. The condition is thought to be due to post-traumatic dysautonomic disturbance.

Carotidynia: It is characterized by spontaneous episodes of dull ache originating in the middle of the neck on one side and radiating to ipsilateral face, ear, jaw, teeth or down the neck, accompanied by

tenderness on palpation over the carotid artery, its bifurcation, and induration of the overlying tissues.

Atypical facial pain: It is constant, unbearably severe, deep seated pain over one or the other maxillary regions, which may radiate either to the mastoid region or down to the neck or across the midline to the opposite maxillary region. Eventually, the pain involves the whole face and the neck bilaterally. It usually occurs in young women.

Miscellaneous Conditions

a. Sudden onset of unilateral facial pain that disappears over a period of days or weeks, with or without associated clinical features of brainstem stroke, occurs in vertebral artery dissection or its occlusion. Sometimes, similar pain which may be more or less persistent, occurs due to compression of the vertebral artery in the neck by a cervical osteophyte,
b. A steady anterior facial pain may be caused by pituitary tumor when it invades the wall of the sphenoid sinus,
c. At times a steady dull pain over the face or temple on one side may precede other symptoms and signs of nasopharyngeal carcinoma.

Pain Occurring in the Neck, Low Back and Limbs

Complaints of pain in the region of the neck, lower part of the back, arms and legs are very frequently encountered in general practice. In some of these cases the diagnosis will be difficult and occasionally impossible. Such pains must always be regarded only as a symptom and not a complete diagnosis. Every attempt should be made to determine their etiology. Cervical and lumbar regions of the spine have maximum degree of dynamic movement and hence these are more prone to trauma and degenerative changes. The vertebral column may be considered as three distinct functional segments—the anterior consisting of the vertebral bodies, their intervertebral disks and longitudinal ligaments: an intermediate segment consisting of the facet joints of the vertebral bodies and their ligaments and a posterior segment which consists of the spinous processes with interspinous ligaments. All these three segments are stabilized by the paravertebral muscles and other structures. Except the bones, all other structures of the spinal column such as the periosteum, ligaments, tendinous attachments of the muscles, synovial membranes of the facet joints and annulus fibrosus of the intervertebral discs are sensitive to pain.

Direct or indirect involvement of the musculoskeletal structures account for the majority of painful lesions. Another important cause is nerve root compression and irritation. It addition, referred pain from thoracic, abdominal and pelvic viscera should also be considered in the differential diagnosis.

Causes of Neck and Back Pain

Musculoskeletal Disorders

i. Congenital anomalies such as spina bifida, sacralization of L5 vertebra, spondylolisthesis and spinal canal stenosis.
ii. Trauma, both acute and recurrent, leading to fractures and subluxation of the vertebrae, sprains, strains and tears of the ligaments, tendons and paravertebral muscles and prolapse of intervertebral disks.
iii. Infections by pyogenic, tuberculous and fungal organisms leading to vertebral osteitis, and epidural or paravertebral abscesses, spinal meningitis and arachnoiditis.
iv. Inflammatory and autoimmune disorders like rheumatoid arthritis and ankylosing spondylitis.
v. Metabolic causes such as osteoporosis, osteomalacia and Paget's disease of bone.
vi. Degenerative conditions of the spine which include spondylosis with osteophyte formation projecting into the intervertebral foramina or narrowing of the spinal canal, prolapsed intervertebral disks and hypertrophied ligamentum flavum.
vii. Primary tumors of the spinal cord, nerve roots (neurofibroma) or meninges (meningioma) and secondary deposits in the vertebrae.

Neurogenic Causes

i. Involvement of spinal nerve root: This may be due to compression by a prolapsed intervertebral disk or tumor, infiltration by leukemic or lymphoma cells, tumors (neurofibroma) and infections such as herpes zoster (acute) and postherpetic neuralgia.

ii. Involvement of nerve plexus in neuralgic amyotrophy, compression by tumors, enlarged lymph nodes or congenital bony anomalies.
iii. Involvement of peripheral nerves by injuries including inadvertent intramuscular injections into or near a nerve, entrapment (carpal tunnel syndrome), nutritional and metabolic neuropathies.

Common Nerve Root Syndromes Caused by Prolapsed Intervertebral Disks

Nerve root compression due to prolapsed intervertebral disks is more common in the lower cervical and lower lumbar levels. Disk prolapses at C5–C6 and C6–C7 spaces in the cervical region and L4–L5 and L5–S1 spaces in the lumbar region account for 90 to 95% of the total disk lesions.

Certain important anatomical differences that exist between the disposition of cervical and lumbar nerve roots in relationship to the inter-vertebral disks, should be kept in mind while considering intervertebral disk prolapse.

1. As there are 8 cervical roots and only 7 cervical vertebrae, C1 root emerges out between the occiput and C1 vertebra. Consequently, other cervical roots emerge above the respective vertebrae. C8 emerges below C7 vertebra. Thereafter the thoracic and lumbar nerve roots emerge below their corresponding vertebrae. For example, L4 root emerges below L4 vertebra at the interspace between L4 and L5, vertebrae.
2. *Due to their shorter and more horizontal course, the cervical roots and their corresponding intervertebral foramina bear a constant relationship, that is C4 root will be affected by a prolapsed intervertebral disk between C3 and C4 vertebrae only. However, in the lumbar region, this relationship is altered because the spinal cord ends at the lower border of L1 vertebra and the lumbar roots have to travel through a long oblique course before they exit from the intervertebral foramina. Hence, a disk lesion at any level in the lumbar region can affect a root anywhere between its origin from the spinal cord and its exit through the intervertebral foramen. For instance, S1 root which has more than 15 cm intraspinal course, may be affected by a disk lesion anywhere along its course.*
3. A nerve root, when it exits through the intervertebral foramen, occupies a higher position in the foramen, than the disk. Hence in the lower lumbar region, a disk lesion does not affect the root that passes through that intervertebral foramen, but it affects a lower one that passes through the interspace below. Thus prolapse of the disk between L4 and L5, vertebrae affects L5 root and not L4 root and a disk lesion between L5 and S1 vertebrae affects the S1 root.

The musculoskeletal causes of pain occurring in this region are given in the section on rheumatology. Table 33.6 shows the clinical features of common monoradicular syndromes.

Neurological Causes of Pain in the Upper Limb

Brachial Neuritis

It produces diffuse, ache-like pain of acute onset in the supraclavicular region, shoulder and the arm. It is usually unilateral. Pain is worse when the limb hangs down and pain is relieved by recumbency. It may be associated with weakness of shoulder girdle muscles.

Thoracic Outlet Syndrome Due to Cervical Rib

This is felt as a dull ache in the distal part of the forearm and the hand, usually on the ulnar aspect, worse in erect posture and relieved by recumbency. It may be associated with weakness and wasting of the hand muscles and trophic changes.

Ulnar Neuropathy

This presents as acute or subacute onset of pain and paraesthesia on the unlar border of the forearm and hand with weakness of the little and ring fingers. Usually this follows trauma or pressure on the ulnar nerve behind the elbow.

Carpal Tunnel Syndrome

This is caused by compression of the median nerve by the flexor retinaculum at the wrist. It leads to pain and paraesthesia in the hand on the lateral aspect, worse during sleep. At times pain may radiate up the forearm and even the arm. Pain is worsened by hyperextension of the wrist. This may be associated with weakness and wasting of the thenar muscles. At times it is bilateral.

Table 33.6: Clinical features of common monoradicular syndromes

Root	*Distribution of pain*	*Sensory deficit*	*Motor deficit*	*Reflex loss*
C6	Along the radial side of forearm, thumb and index finger	Lateral aspect of forearm, thumb and index finger	Elbow flexion, pronation and supination of forearm	Biceps and supinator reflexes
C7	Along the back of the arm and forearm, along the central portion of the front of forearm and middle finger	A linear strip at the center of the front of the forearm and over the middle finger	Shoulder adduction, forearm extension, wrist extension and sometimes wrist flexion	Triceps reflex
C5	Ulnar aspect of forearm, little and ring fingers	Medial aspect of forearm, over little and ring fingers	Flexion and extension of fingers and sometimes flexion of wrist	Finger flexion reflex
L4	Anterior aspect of thigh and knee, provoked by backward bending	Over the medial aspect of the lower part of the leg and over the medial malleolus	Knee extension. Hopping with one leg on the affected side is difficult	Knee reflex, straight leg raising (SLR) test negative
L3	Over the buttocks, along the back of the thigh and lateral aspect of leg up to the lateral malleolus, dorsum and plantar aspect of foot and big toe. Forward bending provokes pain	Over the anterolateral aspect of the leg below the knee and over the dorsum of foot, and big toe	Dorsiflexion of big toe and foot. Walking on heels more difficult than walking on toes	Internal hamstring reflex* (SLR positive)
S1	Over midgluteal region, back of the thigh, and leg up to the heel, along the lateral border of the foot, and fourth and fifth toes. Forward bending provokes pain	Behind the lateral malleolus and along the lateral border of the foot	Plantar flexion of toes and foot	Ankle reflex (SLR positive)

* Internal hamstring reflex: (Semimembranosus and semitendinosus muscles. L5-S1, roots; tibial part of sciatic nerve). Keeping the patient in recumbent position with the thigh slightly abducted and externally rotated, and leg slightly flexed at the knee, place one finger on the medial aspect of the leg just below the knee over the insertion of the internal hamstring muscles and tap on the finger with a hammer. Normal response is further flexion of the leg at the knee and internal rotation of the thigh

Syringomyelia

This may produce diffuse pain in the distal part of one or both upper limbs in some cases.

Dull, Cramp-like Pain

This may be felt in the muscles in motor neuron disease and some types of myopathies. Peripheral neuropathy due to several causes leads to pain and paraesthesia in the area supplied by the nerves. *Early stages of Parkinsonism may manifest as diffuse dull ache in the limbs. Cerebrovascular occlusion leading to hemiplegia may give rise to chronic vague pains on the paralyzed side, as a sequelae.*

Post-traumatic Neuralgia

Following trauma to a peripheral nerve, persistent pain and dysesthesia may occur due to neurinoma formation.

Postherpetic neuralgia

Following herpes zoster, severe burning pain may occur and persist for long periods over the affected area of skin. The pain may be constant or intermittent. Severity of pain varies in different individuals.

History

For proper evaluation of pain, enquire into the following:

1. Mode of onset of pain
2. Circumstances that initiated the pain
3. Relationship of pain to posture and movements
4. Aggravating and relieving factors
5. Associated sensory, motor, sphincter or sexual dysfunctions
6. Co-existing systemic illnesses such as diabetes, tuberculosis, rheumatoid arthritis and others
7. History of trauma in the recent or remote past
8. Details of previous investigations, treatment and their results
9. Psychological and psychiatric history
10. Occupational history.

CHAPTER

34

Investigations in Neurological Diseases

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General investigations, Neurological investigations, Examination of cerebrospinal fluid, Special neurological investigations, Electroencephalography, Magnetoencephalography, Nerve conduction studies, Evoked potentials, Electromyography, Muscle enzymes, Radiological studies, Computed tomography, Magnetic resonance imaging, Positron emission tomography, computed tomography, Echoencephalography, Imaging studies of muscle, Duplex doppler scanning, Histopathological studies

INTRODUCTION

These investigations may be broadly classified into the following varieties:

a. *General investigations:* These are to be undertaken by the family physician at first examination by itself. These give clues to the involvement of the nervous system in systemic diseases such as diabetes mellitus, syphilis or malaria.
b. *Specific investigations:* Investigations such as lumbar puncture, radiography of skull and spine, ultrasonography, computed tomography and magnetic resonance imaging have to be done by the internist, mainly under hospital setting. These help to diagnose conditions such as meningitis, seizures, tumors, abscesses, subdural hematomas, bony lesions of the skull and others.
c. *Specialized investigations:* Investigations such as angiography, myelography, electrophysiological studies, such as electroencephalography (EEG), electromyography (EMG), isotopic tests and biopsy studies which help the neurologist to arrive at the final diagnosis.

GENERAL INVESTIGATIONS

These investigations include the following: Urinalysis for albumin, sugar, phenylalanine, other aminoacidurias, constituents of bile, porphobilinogen and microscopic abnormalities such as excess of erythrocytes and casts.

Biochemical Tests

1. *Blood glucose level*: Hypoglycemia, generally with blood levels below 50 mg/dL gives rise to neuroglycopenia, which manifests as clouding of consciousness, convulsions and coma. When blood glucose level goes above 400 mg/dL the chances to develop hyperosmolar coma increase.
2. *Blood urea, uric acid, creatinine:* These are elevated in renal failure. Uremia leads to several neurological complications and neuropsychiatric abnormalities.
3. *Blood ammonia level:* It is elevated in hepatic failure, which may be the cause of neuropsychiatric complications in acute or chronic liver disease.
4. Abnormal increase of *amino acids* in urine are found in several metabolic disorders, e.g. *phenylketonuria.*
5. Reduction in the blood levels of *cerculoplasmin* and elevated levels of *serum copper* in blood and tissues is a diagnostic finding in hepatolenticular degeneration (*Wilson's disease*).
6. *Muscle enzymes* like creatine phosphokinase and aldolase are increased in muscle dystrophies.

Several neurological abnormalities can be diagnosed by biochemical investigations. The reader should refer to textbooks on neurology for a complete list.

Hematology

Hemoglobin level

Anemia leads to headache, giddiness, throbbing in the head, syncope and retinal changes such as hemorrhage and papilloedema. These are more pronounced when the hemoglobin level drops below 6 g/dL. These clear up when the hemoglobin level is restored to normal.

Total and Differential Leukocyte Counts

Acute leukemias, particularly acute lymphatic leukemia leads to neurological involvement which may present clinically with the picture of meningitis, raised intracranial tension, convulsions, retinal hemorrhages, tumor formation and various forms of paralysis. In children with rapidly progressing neurological abnormalities, neuroleukemia should be kept in mind.

Neutrophil leukocytosis may accompany bacterial meningitis. Lymphocytosis in the presence of meningitis may suggest viral etiology or tuberculosis.

Platelets

Thrombocytopenia from any cause may lead to intracranial hemorrhage if the platelet count falls below 20,000/cmm. In fulminant purpura and disseminated intravascular coagulation, intracranial bleeding is a fatal complication.

Coagulation tests

Both therapeutic anticoagulation and natural coagulopathies may be complicated by intracranial bleeds. In such cases parameters to assess the hemostatic profile, e.g. bleeding and clotting times, prothrombin time, partial thromboplastin time, assays of coagulation factors, studies of platelet number and function and excessive fibrinolysis are to be undertaken.

Hypercoagulable states

Thrombocytosis, thrombocythemia, hyperviscosity states, dehydration and congenital deficiency of naturally occurring antithrombotic substances like protein C and protein S lead to venous and arterial thrombosis in the CNS. Management of these cases is the realm of the hematologist. Several hematological diseases such as sickle cell anemia and leukemias lead to neurological syndromes.

Serological tests

Both syphilis and AIDS are common to produce neurological complications and therefore, routine testing is indicated in a suspected case-VDRL in the serum or CSF for syphilis and Elisa and Western blot tests for AIDS.

Parasitology

Falciparum malaria, trypanosomes, and cysticerci are common to involve the CNS. Malaria and trypanosomiasis can be diagnosed by blood smear examination. Cysticercosis can be diagnosed by serological tests and the presence of these cysts in the brain, which will be revealed by CT scan, but better by MRI.

NEUROLOGICAL INVESTIGATIONS

Lumbar Puncture

Lumbar puncture (LP) is performed to obtain samples of cerebrospinal fluid (CSF) for analysis, introduce therapeutic or investigational agents into the lumbar subarachnoid space and for measuring CSF pressure. It is an invasive procedure. With the advent of CT and MRI scans, many neurological centers have reduced the number of lumbar punctures, especially when diagnostic information can be obtained otherwise and when the procedure is likely to be risky. However, general physicians have to perform this procedure in many patients with neurological disorders since it helps to arrive at the diagnosis and it can be performed even in moderately equipped hospitals. At times the procedure can be hazardous and therefore, great care has to be taken in patient selection and performance of the procedure. In centers where facility for computed tomogram (CT) is available, it is better to make a preliminary assessment of the intracranial pathology before undertaking lumbar or cisternal punctures when judiciously employed and skillfully performed. It is one of the most valuable diagnostic procedures in neurology. Hence, every trainee in internal medicine has to be conversant with this procedure.

Indications for LP

1. To confirm the diagnosis of meningitis, encephalitis, neurosyphilis and other infections when clinical picture is suggestive.
2. To rule out or confirm subarachnoid hemorrhage when computerized tomography imaging facilities are not available, and when meningitis has to be excluded.
3. Suspected involvement of CNS in leukemia and lymphoma.
4. Guillain-Barré syndrome, multiple sclerosis, some cases of peripheral neuropathy and transverse myelitis.
5. Idiopathic intracranial hypertension.
6. Normal pressure hydrocephalus.
7. To introduce contrast agents such as iodinated dyes into the subarachnoid space for getting myelograms and other imaging procedures such as isotopic studies and CT scaning.
8. To introduce therapeutic agents into CSF, e.g. antibiotics for meningitis, antileukemic drugs in acute lymphatic leukemia and others.
9. To administer spinal anesthesia.
10. As a therapeutic measure to reduce intracranial pressure in idiopathic intracranial hypertension, neonatal intraventricular hemorrhage, and hydrocephalus complicating meningitis.

Contraindications for LP

1. Sepsis at the site of lumbar puncture. The infection may spread into CSF and lead to maningitis.
2. Possibility of raised intracranial pressure, particularly due to intracranial space occupying lesions. If CSF is released from below in the presence of raised intracranial tension, downward herniation of brain occurs leading to pressure effects and reduction in blood supply of the brainstem, resulting in respiratory paralysis and death. This is known as 'coning effect'. The common structures that herniate are the uncus of the temporal lobe through the tentorium cerebelli and cerebellar tonsils into the foramen magnum.
3. Possibility of spinal cord compression: Sudden release of CSF pressure from below may worsen cord compression in cases of spinal tumors, edema or infection of the cord and others.
4. Hypersensitivity to the drugs and anesthetic agents employed.

Note: Absence of papilloedema does not always exclude increased intracranial pressure caused by intracranial space occupying lesion. Therefore, if the latter condition is suspected clinically, a CT scan of the head should be done prior to LP.

However, idiopathic intracranial hypertension is one condition where measurement of CSF pressure is the confirmatory test and even in the presence of severe papilloedema, if CT scan rules out space occupying lesion, LP has to be performed. In idiopathic intracranial hypertension coning of the brainstem is rare. In all difficult and potentially dangerous situations, it is preferable to perform LP only in centers where neurosurgical help is available to tackle the postlumbar puncture complications. It should be remembered that conditions like meningitis and encephalitis where delay in specific treatment may lead to mortality or severe morbidity, LP should not be delayed, since CSF examination is the gold standard of diagnosis. If there is any contraindications or LP cisternal puncture should be done to collect CSF.

Procedure of LP

Explain the procedure to the patient and relatives and get informed consent. The LP should be done under strict aseptic precautions as for a minor surgical procedure.

i. *Position of the patient:* Make the patient lie on the edge of a hard bed on his left side with his back perpendicular to the bed. Keep him in 'fetal' position, i.e. knees drawn up towards the chest and the head flexed, so as to widen the interspinous spaces maximally.

ii. *Preparation of skin at the puncture site:* Expose his back from mid thoracic to mid gluteal region. The skin is thoroughly cleaned in turn with spirit, iodine and spirit or providone iodine. Drape the area with sterile towels, exposing only the area to be punctured.

iii. *Localization of the puncture site:* LP is done usually through the interspinous space between L3-L4 or L4-L5 vertebrae. In infants, the L4-L5 space is selected due to low placement of the conus medullaris. The L3-L4 space can be easily identified as it lies just below the line

joining the highest points on the iliac crests. Select this interspace and mark it.

iv. *Local anesthesia:* It is produced by injecting about 2 mL of 2%, lignocaine solution, first into the skin and then into deeper tissues. Start the LP only after ensuring that the spot is anesthetized.

v. *Insertion of* LP *needle:* The LP needle is a special hollow needle about 8 cm long with a sharp, short bevel at its tip and provided with its style. LP needles are available in sizes of 9, 18, 20 and 21 gauge. The higher the number, smaller the bore and length of the needle. For an average sized adult, 18 or 19 gauge needle should be used. For children, 20 or 21 gauge is to be preferred.

Stretch the skin over the site of puncture at the same time feeling for the interspace with the tip of your left thumb. Insert the LP needle containing the stylet keeping the bevel parallel to the long axis, so that the needle tip only splits the longitudinal fibers of ligamentum flavum and the dura mater, without cutting them. Push the needle firmly inwards keeping it exactly in the midline slightly towards the head at right angles to the body curvature.

The position and direction of the needle movement are crucial to get successful LP. If the needle gets deflected or encounters bony resistance, withdraw the needle up to the subcutaneous tissue and reintroduce it at a different angle. Do not change the direction of the needle when it is midway in the deeper tissues. When properly introduced to a depth of about 4.5 cm a slight resistance will be felt due to ligamentum flavum. A feeling of 'giving way' indicates puncture of this ligament, the dura mater and entry of the needle tip into subarachnoid space. At this stage, remove the stylet. When LP is successful, the CSF flows out as the stylet is removed. Allow only a few drops of the fluid to escape and re-insert the style immediately. The patient is made to lie relaxed with his legs extended, head straight and breathing freely. If no CSF emerges, slowly withdraw the needle 1 to 2 mm by rotating it. This will help to clear any obstruction to the needle tip, and start CSF flow. If the patient feels a sudden shooting pain in one lower limb, it indicates that a sensory root has been touched by the needle tip, and that the needle tip is too far away from the midline.

If no CSF emerges, refix the stylet, advance the needle a bit more and then remove the stylet to see CSF flow. If you feel that you have entered the subarachnoid space by the 'giving way' feeling on the needle, but still no CSF is coming out, perform Queckenstedt's test to raise spinal CSF pressure and promote flow. If this is also unsuccessful withdraw the needle up to the subcutaneous tissue and reintroduce it in a different direction. If two or three attempts fail, try the procedure through the adjacent interspinous space or defer the procedure to a subsequent occasion and perform LP preferably after sedating the patient.

An alternate position to do LP is with the patient sitting up with his legs hanging by the side of the couch, and leaning forward over a pillow held firmly in front of his abdomen, so that his face touches his thighs. In this position, the interspinous spaces are widened maximally. Once the LP needle has reached the subarachnoid space and CSF comes out, the patient is made to lie in the lateral decubitus. CSF pressure is measured and further procedures done in this position.

Sometimes when the CSF pressure is too low, as in severe dehydration, the fluid may not come out spontaneously. In such cases perform Queckenstedt's test to get more fluid. If the CSF is very thick due to purulent inflammation, it may not flow out through a narrow needle.

vi. *Measurement of CSF pressure:* In all cases where abnormalities of CSF pressure are suspected, manometry should be done to measure the CSF pressure. The patient should be in the lateral decubitus with the head and sacrum at the same level and the legs fully extended, and breathing freely. The LP manometer is a calibrated glass tube with 1 mm bore, 30 em long and provided with a reservoir at its top. It is connected to the LP needle through an adapter, allowing only minimal CSF to escape during the procedure.

Normally the opening pressure is about 60 to 150 mm of CSF, with 1 to 2 mm oscillation, synchronous with each pulse and 1 to 2 cm fluctuation with each respiration. The pressure as seen in the manometer is recorded.

Pressures between 130 to 200 mm of CSF are borderline increases and above 200 mm are definitely abnormal. Fallacies occur if the patient

is tense and not fully relaxed or the head is flexed, thereby the jugular veins are compressed. These factors should be corrected before taking the final reading. If the pressure is genuinely elevated, disconnect the manometer and withdraw the LP needle after inserting the stylet. The CSF obtained from the manometer can be used for further tests. If the pressure is normal or low Queckenstedt's test is done before disconnecting the manometer.

Even while doing LP note the rate of flow of CSF, its color and consistency and the responses to Queckenstedt's test. If possible, collect the first few drops directly on glass slides for examining the cellular content and for Gram staining in the case of purulent CSF or opalescent CSF.

Queckenstedt's test: This test is employed to determine whether there is spinal block, i.e. any block between the intracranial and lumbar subarachnoid space. In conditions such as intramedullary or extramedullar tumors in the spinal canal and spinal arachnoiditis, spinal block may develop.

With the patient lying in the lateral decubitus, and CSF flowing freely through the LP needle or during spinal manometry, compress the internal jugular vein of one side at the root of the neck for about 10 seconds. This hinders venous return from the intracranial venous sinuses and thus elevates intracranial pressure. This rise is reflected in the lumbar subarachnoid space as a rise in pressure in the manometer or more rapid flow of CSF. Subjectively, increase in flow can be observed by counting the number of drops in five seconds before and after the procedure. On releasing the compression in the neck, the CSF flow returns to the original rate. If the spinal block is total, there will be no rise of pressure in the lumbar subarachnoid space on performing the test. In the early stages, when the block is partial, the rise in pressure may be prompt, but the fall on releasing jugular compression is unduly delayed.

If the lateral or sigmoid venous sinus of one side is occluded by thrombus, there will not be rise of intracranial pressure on compressing the jugular vein on that side. Queckenstedt's test is contraindicated in the presence of raised intracranial pressure.

Collection of CSF: While performing LP, the CSF should be collected for the following tests, as per the clinical indications. In all about 5 mL of CSF may be collected in three sterilized containers.

CSF EXAMINATION

Microscopic Examination (Table 34.1)

1. *Cell count:* Normal CSF is clear like water, colorless and contains only up to 2 to 5 lymphocytes per cmm. Pleocytosis is the

Table 34.1: Diagnostic features of CSF in the common forms of meningitis

Test	*Normal*	*Meningitis*				
		Pyogenic	*TB*	*Viral*	*Fungal*	*Syphilitic*
Appearance	Clear colorless	Turbid	Clear or slightly opalescent	Clear	Clear	Clear
Pressure	60–150 mm of CSF	Raised	Raised	Raised	Raised	Raised or N
Proteins	20–40 mg/dL	500–1000 mg/dL	300–400 mg/dL	180–200 mg/dL	up to 200 or more	80–100 mg/dL
Sugar	40–80 mg/dL	below 40	below 40	normal	reduced	normal
Chlorides	720–750 mg/dL	reduced	Considerably reduced	normal	reduced	normal
Cells	0–5/cmm, all lymphocytes	1000/cmm or more, mostly neutrophils	150–200/cmm or or more, mostly lymphocytes	100–200/cmm or more mostly lymphocytes	100–200/cmm or more mostly lymphocytes	100–200/cmm or more mostly lymphocytes
Culture	Sterile	Organisms isolated	*Mycobacterium* in 20–30%	Viruses may be isolated	fungi can be grown	*Treponema* can be demonstrated or grown by special techniques
VDRL	–ve	–ve	–ve	–ve	–ve	+ve

presence of excessive number of leukocytes. When more than 200 cells/cmm are present, the fluid may become opalescent. Presence of more than 1000 cells/cmm makes it frankly turbid and purulent. Purulent CSF is suggestive of bacterial meningitis and the predominent cells are neutrophils. Morphology of the cells can be made out by wet-staining with methylene blue. Absolute count can be done as is done for WBC in a Fuchs-Rosenthal counting chamber. CSF pleocytois may be due to lymphocytes, granulocytes or mixed. Presence of excess cells is the most definite diagnostic evidence of meningitis. In infiltration of the central nervous system by leukemia, lymphoma and carcinomas, the corresponding abnormal cells appear in CSF.

2. *Gram staining:* This is the most easy and readily available rapid method to diagnose the presence of bacterial meningitis and identify the organism. In all cases of purulent meningitis this should be done. Morphological identification of the organism *(Pneumococcus, Streptococcus, Meningococcus, H. influenzae* and *E. coli)* helps to institute specific antibiotic therapy without delay. Acid fast staining of the cobweb formed in the CSF in TB meningitis may reveal mycobacteria. India ink staining reveals *Cryptococcus*.

Biochemical Tests

Protein content, glucose, chlorides, immunoglobulins and several others can be estimated. Normal CSF contains 20 to 40 mg/dL proteins, 60 to 80 mg/dL glucose and chlorides depending on the serum chloride level.

Proteins: Moderate to high rise in protein content occurs in inflammatory conditions such as meningitis and encephalitis. Maximum elevation occurs in spinal block and Guillain-Barré syndrome. In infective lesions the protein content and cell count rise together, whereas in spinal block and Guillain-Barré syndrome proteins increase without corresponding rise in cells (albuminocytological dissociation).

Glucose: CSF glucose levels vary directly with the blood glucose level. Generally the CSF glucose is 20 to 30 mg below the blood glucose levels, if the specimens are taken at the same time. Disproportionate fall in CSF glucose occurs in all types of bacterial meningitis. In tuberculous meningitis, substantial reduction of CSF glucose is a very valuable diagnostic clue which helps to arrive at the provisional diagnosis early. In viral meningitis, encephalitis and neuroleukemia in which lymphocytes may be seen in excess, the CSF glucose is not diagnostically altered.

Chlorides: The CSF chloride levels vary directly with the blood chloride levels. Low CSF chloride levels occur in dehydration and electrolyte depletion. It is not of specific diagnostic importance.

Immunoglobulins: Identification and estimation of IgG may help in the diagnosis of multiple sclerosis, sarcoidosis and connective tissue diseases. Normally IgG in CSF is 6 to 12% of the total proteins. Values above 20% are abnormal. Electrophoresis of CSF may reveal oligoclonal bands in the gamma globulin region in multiple sclerosis.

Note: Normal CSF does not show any coagulum or clot on standing. In tuberculous meningitis and some forms of viral meningoencephalitis, the CSF may show a 'cobweb' like precipitate on keeping at room temperature for 12 to 24 hours. Staining of the cobweb may show acid fast bacilli in 20 to 30% of cases of tuberculous meningitis.

Frank coagulation of CSF on standing occurs when the protein content is very high. This may occur in spinal block and Guillain Barre syndrome. The combination of xanthochromia (yellow color), spontaneous clotting and albuminocytological dissociation of CSF is called Froin's syndrome.

Microbiological Test

CSF has to be sent for culture of bacteria, fungi and viruses. Etiological diagnosis of infective lesion can be made by this method. Cultures for M. *tuberculosis* take about 4 to 6 weeks to grow. Therefore, newer methods such as immunofluorescence or DNA techniques like polymerase chain reaction (PCR) have been devised.

For demonstrating cryptococcus in CSF, a simple method is to mix equal amounts of CSF and India ink; and examine the wet preparation under high power of the microscope. Cryptococci are seen as refractile dots with a clear circular zone around.

Several other tests are available which are to be employed by the neurologist under particular circumstances.

Blood Stained CSF

This may be due to injury to one of the veins during LP or it may be due to subarachnoid hemorrhage. These can be easily distinguished by the points given in Table 34.2. In subarachnoid hemorrhage, the erythrocytes break down releasing bile pigments which stain the CSF yellow. This is seen about 6 hours after the bleed.

Complications of LP

1. *Coning of the brainstem:* This should be suspected if:
 a. The patient becomes less alert
 b. The pupils start dilating
 c. The respiration becomes shallow and slower.

 To avoid this, the patient should be made to lie prone soon after LP and the foot end of the bed raised by 45 cm by suitable blocks under the cot.

 If coning is suspected, immediately give 20%. mannitol 200 mL intravenously rapidly and summon the help of a neurologist or neurosurgeon.
2. *Postlumbar puncture headache:* This is due to disturbance of CSF hemodynamics and leak of CSF into extradural space. This is minimized by using the smallest bore needle for LP. The headache stops spontaneously over hours. Sometimes, it may be prolonged and distressing. Analgesics may help, so also rehydration of the patient and reassurance.
3. Infection and secondary meningitis is a rare, but grave complication. This should be avoided by strict aseptic precautions.
4. Chemical meningitis may result from irritation by the drug introduced into the CSF.

Table 34.2: Differentiation in CSF between traumatic bloody tap and subarachnoid hemorrhage

Findings	*Traumatic blood staining*	*Subarachnoid hemorrhage*
1. Observation of CSF on flowing from the LP needle or if it is collected in 3 successive tubes	Tends to become clearer	Uniform blood staining
2. CSF is kept at room temperature for 1 hour	The blood clots	Does not clot, but the erythrocytes settle to the bottom. In SA hemorrhage defibrination takes place.
3. Supernatant fluid observed after centrifuging for 2 minutes at 3000 RPM, soon after obtaining the CSF	Supernatant is colorless	Supernatant is xanthochromic due to the presence of bile pigment

Alternative Methods to Obtain CSF

When examination of the CSF is mandatory and absolutely necessary to establish the diagnosis, but where the LP fails repeatedly, CSF can be obtained by cisternal puncture or cerebral ventricular puncture. Sometimes cisternal puncture is done to introduce dye to delineate the upper level of spinal block.

SPECIAL NEUROLOGICAL INVESTIGATIONS

	Tests for structural integrity	*Tests for functional integrity*
Brain	Computed tomography (CT) Magnetic resonance imaging (MRI) Cerebral angiography (conventional) Digital subtraction angiography (DSA) MRI angiography Transcranial doppler study Radioisotope scan Echoencephalography Electrogencephalography by (PEG)	Electroencephalography (EEG) Evoked potential study (EP) Brain electrical activity mapping (BEAM) Single photon emission computed tomography (SPECT) MRI spectroscopy Positron emission tomography (PET)
Brain biopsy		
Spinal cord	CT scan MRI scan Myelography	Evoked potentials (EP)
Nerve	Nerve biopsy	Nerve conduction velocity (NCV) study, Evoked potentials
Muscle	Muscle biopsy	Electromyography (EMG)
Neuromuscular junction		Muscle enzymes-CPK and LDH Repetitive, electrical nerve stimulation

General Considerations

Many diseases of the nervous system demand specialized investigations to know the structural and functional abnormalities and to help in the diagnosis, management, follow-up and prognosis. Since many of these investigations require costly equipment and experienced personnel these are available only in a few places in India. Therefore, there is great need to select the appropriate investigation in a cost effective manner. The following account gives a brief description of various investigations available with their indications, advantages and limitations. Any investigation in a given patient will give either normal results or reveal some abnormalities. The interpretation of these results also has to be done in the light of the clinical settings.

ELECTROENCEPHALOGRAPHY

Electroencephalography (EEG) is a specialized neurological investigation which involves recording of the spontaneous electrical activity of the brain from the scalp. This is a safe, noninvasive, relatively inexpensive, painless, easily repeatable procedure to know the functional status as opposed to the CT or MRI scan which reveals the structural integrity of the brain. Since the EEG findings in many of the cerebral disorders are nonspecific, its diagnostic value is confined to a few conditions such as epilepsies, encephalitides, metabolic, toxic, anoxic and drug induced encephalopathies and in the study of sleep disorders.

The modern EEG machine has 8 to 16 channels to record the brain activity simultaneously from many areas of the scalp. Electrodes, which are usually silver chloride disks are applied to the scalp, by means of an adhesive material which also provides good electrical contact between the electrode and the skin, after the hair and the scalp are cleaned of oil and grease. The placement of these electrodes on the scalp is standardized internationally (10–20% system). The tracing is recorded on a moving sheet of paper for about 30 to 60 minutes during the awake state, while the patient comfortably lies in a quiet room. The patient need not fast for this test nor miss his medication, including the anticonvulsants. Ideally the first EEG may be taken after sleep deprivation in suspect cases of epilepsy. In many laboratories, hyperventilation for 3 minutes and photic stimulation at different rates with a flickering light (strobe) are used as provocating procedures.

The EEG tracing is studied to note the frequency, amplitude, morphology and topography of the brain electrical activity. Four types of frequency bands of EEG are encountered. They are: (i) delta (less than 4 Hz activity), (ii) theta (4-8 Hz), (iii) alpha (8-13 Hz), and (iv) beta (more than 13 Hz) bands.

The EEG of a normal adult in the awake and resting state with eyes closed consists of alpha rhythm of 30 to 60 microvolts over the posterior regions of the head. In children, the frequency is slower in the theta or delta range, depending on the age.

The abnormalities in the EEG may be in the form of asymmetrical activity, faster or slower frequency activity, low or high amplitude activity or abnormal wave forms like sharp waves, slow waves and/or spikes. Localized or focal abnormalities, though highly significant, cannot reliably distinguish an underlying pathological lesion such as tumor, abscess, hematoma or infarct.

EEG is of greatest value in seizure disorders not only to document the interictal subclinical seizure activity but also to classify the epilepsy as partial or generalized, depending on whether the seizure activity is focal or generalized. Sporadic spikes, sharp waves, spike and slow wave complexes or 3 Hz spike and wave complexes in petit mal epilepsy are some of the EEG patterns, which are diagnostic (Figs 34.1A and B). However, it should be mentioned here that a normal interictal EEG does not exclude epilepsy because in only 50 to 60% of these patients EEG will be abnormal.

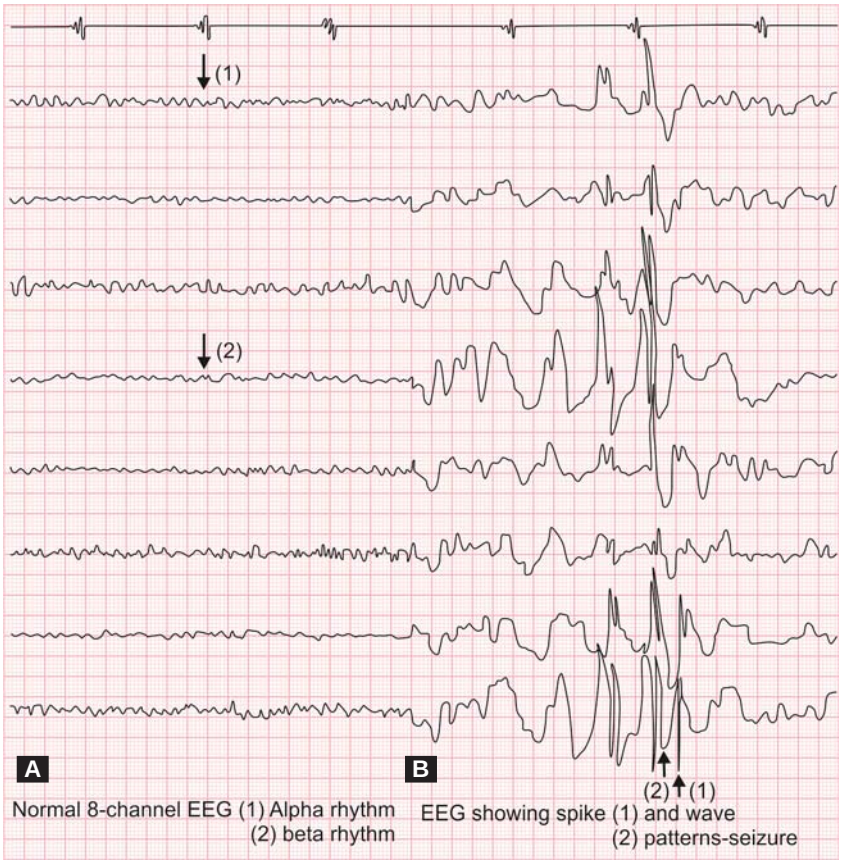
The characteristic periodic EEG complexes in subacute sclerosing panencephalitis and Jacob-Cruetzfeldt disease, the triphasic waves in hepatic coma and the electrocerebral silence in brain death are some of the other diagnostic EEG patterns.

Video Encephalography

Video encephalography is a more useful technique to detect intermittent seizure activity and distinguish between organic and functional diseases.

MAGNETOENCEPHALOGRAPHY

Unlike EEG, magnetoencephalography (MEG) detects the magnetic fields emanating from the brain tissue. It is much more sensitive than EEG in



Figs 34.1A and B: Normal EEG and EEG in seizure

detecting deep seated small pathological lesions in the brain. However, it is very expensive and hence is not easily, available for clinical studies.

NERVE CONDUCTION STUDIES

Nerve conduction study is employed to test the integrity of a peripheral nerve. The presence or absence of denervation, the site of nerve block if any, and nature of the lesion such as demyelination or axonal lesions can be detected easily even if the patient is not cooperative. Hence this test can be employed in infants, children and in comatose patients.

Nerve conduction velocity studies (NCV) are of two types:

i. Motor nerve conduction velocity (MNCV) study
ii. Sensory nerve conduction velocity (SNCV) study.

In motor nerve conduction studies, a stimulating surface electrode is placed on the skin overlying a peripheral nerve and a brief electric shock, slightly greater than that required to produce a maximal contraction of the innervated muscle (supramaximal stimulus) is given to produce muscle contraction. The action potential generated by the contracting muscle is picked up by recording electrodes placed on the skin over the muscle and this is displayed on a cathode-ray oscilloscope for analysis. The action potential of the muscle occurs a few milliseconds after the stimulus is delivered (stimulus artefact). The time taken for the stimulus impulse to travel along the nerve and the neuromuscular junction from the stimulation artefact to the beginning of the evoked muscle action potential is called latency, and it is measured in milliseconds. The duration and amplitude of the evoked muscle action potential are also measured.

For determining nerve conduction velocity, the same nerve is stimulated at two points along its course. The difference in the latency times of these two stimuli gives the conduction time between the

two points of stimulation. The distance between these two sites is measured and the NCV calculated as meters/ second. Normal is 50 to 60 m/sec.

NCV studies are valuable (i) to detect demyelination in the peripheral nerves where the NCV will be significantly slowed down (ii) to detect axonal lesion where the NCV may be within normal limits but the evoked muscle action potential will be of abnormally low amplitude and longer duration. NCV study also helps to localize the site of pathology in the peripheral nerves.

Using special techniques, it is also possible to study electrophysiologically the integrity of the proximal portion of the nerve roots and the reflex arc.

Routinely, motor nerve conduction studies are performed on median and ulnar nerves in the upper limbs and the lateral popliteal nerves in the lower limbs.

Sensory nerve conduction studies are performed by stimulating the sensory nerves distally and picking up the nerve action potentials proximally. Being very small in amplitude, these potentials have to be amplified to a greater degree and averaged through a computer to make them more discernible. The common sites selected for distal stimulation are the index finger for the median nerve, the little finger for the ulnar nerve, and below and in front of the ankle for the sural nerve (Table 34.3).

Normal Values for Nerve Conduction

Nerve conduction velocities at birth are about 50% of normal adult values, increasing rapidly to about 75% by 1 year and reach adult values by about 4 to 5 years of age. There is gradual slowing of conduction velocities as the age advances (3% decline per decade after 30 years) with a steep decline after the age of 60 years. Upper extremity nerve conduction velocities are generally 10 to 15% faster than those of the lower extremity nerves. Sensory nerve conduction time is about 5% faster than motor conduction time.

For diagnozing neuromuscular disorders, such as myasthenia gravis, a peripheral nerve such as median or ulnar nerve or the brachial plexus at the Frb's point in the neck is stimulated by delivering a series of supramaximal stimuli and the evoked response is recorded from the corresponding muscles. A significant decrease in the amplitude of the third or fourth evoked muscle response as compared to the first response suggests myasthenia gravis. This phenomenon is known as decremental response. In Eaton-Lambert syndrome there is significant increase in action potential with repeated stimulation.

EVOKED POTENTIALS

It is possible to study the functional integrity of the sensory pathways from the periphery to the cerebral cortex by stimulating the peripheral sensory nerves or their receptors. Electrical potentials (EP) which are generated in the central nervous system are called evoked potentials. Those commonly employed include:

1. *Visual evoked potentials* (VEP), elicited by stimulating the rods and cones in the retina by

Table 34.3: The normal values for the commonly studied nerves in adults

Nerve	*Distal Latency (Milli seconds)*	*Amplitude (Peak to Peak)*	*Maximum conduction Velocity (Meters/sec)*
Ulimar (motor)	3.0	5 mv	50
Ulnar (Sensory)	3.2	5 μv	51
Median (motor	3.8	5 mv	50
Median (sensory)	3.5	10 μv	51
Radial (motor)	2.9	7 mv	52
Radial (sensory)	3.3	15 μv	50
Peroneal (motor)	5.0	4 mv	44
Tibial (motor)	5.1	5 mv	43
Sural (sensory)	4.4	5 μv	40
H-reflex latency	35	-	-
F-wave latency		-	-
Upper limbs	30	-	-
Lower limbs	50	-	-

Note: However, it should be remembered that the normal values may vary from laboratory to laboratory because of differences in the techniques used

a flash of light, or more commonly by a checker board pattern on a TV screen.
2. *Auditory evoked potentials* (AEP) elicited by stimulating the ears by clicks through head phones
3. *Somatatosensory evoked potentials* (SSEP) produced by stimulating the peripheral nerves with electrical current.

The evoked electrical potentials, which are of very low amplitude are averaged by a computer and amplified by special equipment. These amplified potentials are picked up by surface electrodes on the scalp or over the spine in the case of SSEP. By knowing the normal time taken for the impulse to travel from the site of stimulation to the cortex (latency) it is possible to find out in a given patient, whether his EP latencies are normal or not. If abnormal, it is also possible to localise the site of abnormality in the sensory pathways. The advantage of these studies is that they do not depend on subjective sensations by the patient and also they can be performed in comatose individuals, in infants, children and uncooperative adults under sedation.

ELECTROMYOGRAPHY

Electromyography (EMG) is an investigation in which the electrical activity of muscle is recorded through a needle electrode inserted into the muscle and it is displayed on a cathode ray oscilloscope and played over a loud speaker for simultaneous visual and auditory analysis. Usually this is performed by the neurologist and is associated with some amount of discomfort to the patient because of multiple needle insertions into the muscle.

Basically it is carried out to know whether a muscle is normal or shows evidence of myopathy or neurogenic lesion, both of which can lead to muscle weakness and wasting. A normal muscle is electrically silent when it is at complete rest.

When it contracts minimally voluntarily, the action potentials of motor units that are activated appear on the oscilloscope which have a certain configuration, amplitude and duration. With more and more vigorous voluntary contraction, the number of these action potentials increases and during maximal contraction which recruits all the motor units for contraction, these potentials merge with each other to give full recruitment pattern. When the muscle contraction ceases, again the muscle becomes electrically silent.

When a muscle becomes weak due to a primary muscle disease like myopathy, its EMG pattern differs from that of a normal muscle. When the affected muscle is at rest, there will be spontaneous electrical activity in the form of fibrillation potentials. During minimal voluntary contraction, the generated action potentials will be of lower amplitude and shorter duration as compared to a normal muscle and during maximal contraction, the recruitment potentials will be full. As against this, a muscle which is weak due to a neurogenic lesion, i.e. its neural connection to the anterior hom cells of the spinal cord is affected, it shows spontaneous electrical activity at rest in the form of fibrillation and fasciculation potentials and during minimal voluntary contraction, the action potentials will be of larger amplitude and longer duration than normal and during maximal contraction, the recruitment potentials will be less than normal.

Thus, EMG helps to differentiate muscle weakness due to a primary muscle disease from that due to a nerve or anterior horn cell disease. But it does not indicate the causes or etiology of the diseases for which other supplementary investigations are required. Many a time it is possible to distinguish primary myopathy from neuropathy clinically, but occasionally it is difficult. EMG is most valuable to distinguish such cases. Characteristic EMG pattern occurs in myotonic disorders (dive bomber sound) and EMG also helps to differentiate true myotonia from pseudomytonia and true weakness from hysterical weakness. Muscle enzyme levels like creatine phosphokinase (CPK) and lactic dehydrogenase (LDH) in the serum may transiently increase, following an EMG investigation because of the needle trauma to muscles. Therefore, the blood samples for estimation of these enzymes should be collected before performing the EMG.

MUSCLE ENZYMES

There are several enzymes in the muscles which will be released into circulation whenever there is injury to the muscles. Of these, **creatinine kinase (CK)** is the most important one. The CK is an enzyme found primarily in skeletal muscles, heart and brain with concentration in skeletal muscles being more

than 3 times that in the heart and brain. There are 3 forms of CK isoenzymes - MM (skeletal muscles), MB (cardiac muscle), and BB (brain). Normal adult skeletal muscle contains about 95% MM and 5% MB. The normal serum CK concentration is < 130 u/L.

Muscle damage due to any cause significantly elevates CK levels in the serum. It should be remembered that normal exercise, an IM injection or even EMG examination with needle electrodes may elevate CK levels as much as 3 to 8 fold which may take 24 to 48 hours to return to normal level.

Marked CK elevation occurs only in polymyositis or dermotomyositis, some types of muscular dystrophies and hypokalemic myopathy. Serum CK is also elevated in acute myocardial infarction, collagen vascular disease, burns, chest trauma, status epilepticus, brain infarction, hyperthermia, hypothyroid myopathy, alcoholic myopathy and after surgery. Certain drugs like lovastatin, clofibrate and aminocaproic acid may elevate serum CK level.

An elevation of serum CK is a much more sensitive determinat of muscle damage than elevation of any other muscle enzyme (e.g. LDH, aldolase).

RADIOLOGICAL STUDIES

Plain X-rays

Plain X-rays of the skull and the spine are very useful investigations in traumatic lesions, surgical problems, malignancies and similar conditions. Their ready availability in almost all parts of India is of considerable advantage.

Skull X-rays detect osteolytic lesions of the skull vault as is seen in metastatic deposits and multiple myeloma, osteosclerotic changes as in Paget's disease and meningioma, fractures due to head trauma, infections like osteomyelitis, bony erosions of the petrous temporal bone in acoustic neuroma and enlargement of the foramina at the bases of the skull. Increased intracranial tension can be diagnosed by beaten silver appearance of skull vault, separation of cranial sutures in children and erosion of the dorsum sella.

Unilateral supratentorial space occupying mass lesions like tumors, abscesses and cysts may be suspected from X-rays since they may produce abnormal calcification or shift of the calcified falx cerebri and/or pineal gland across the midline in a few cases. Enlargement of the pituitary fossa caused by a pituitary tumor, thickening of the skull vault in acromegaly, and abnormal calcification in tuberous sclerosis and Sturge-Weber syndrome can all be detected by skull X-rays.

X-rays of the vertebral column are indicated whenever lesions are suspected in the vertebrae, spinal cord, spinal roots or the adjacent tissues. Routinely, both anteroposterior (AP) and lateral views are obtained. In the cervical and lumbar regions, additional right and left oblique views are required because the intervertebral foramina are seen well only in the oblique pictures. While ordering for X-ray of the spine, the particular region of interest should be specified so that this portion can be focussed properly in the picture.

Knowledge of the relationship between vertebral bodies and spinal segments helps to specify the vertebrae to be imaged and correlate the neurological defect with the vertebral lesion.

Contrast Radiography

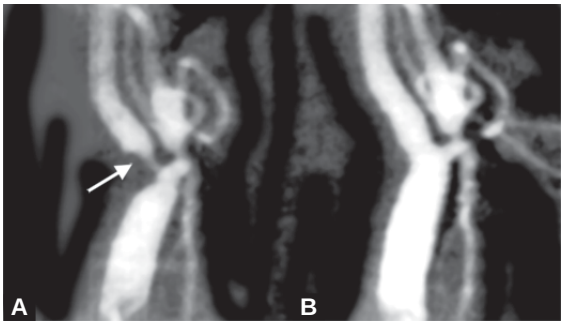
These were the only methods to directly visualize the brain and spinal cord before the advent of CT scan and further imaging procedures. Myelography using radio-opaque dye is done to delineate abnormalities in the cord such as cord compression, tumors, vascular malformations and others. These invasive methods have been replaced by MRI at present.

Air encephalography, ventriculography and other invasive procedures have been almost totally replaced by CT and MRI.

Cerebral Arteriography

This is the technique by which the cerebral blood vessels are radiologically visualized. Its use has drastically come down with the introduction of CT. However, it is the most important investigation whenever an abnormality in the cerebral vessels is suspected such as aneurysm, arteriovenous malformation and arteritis (Figs 34.2 and 34.3).

It is also indicated in certain brain tumors such as meningiomas, to assess their vascularity and in patients with TIA due to occlusive carotid artery disease, prior to their surgical management. Cerebral arteriography can be performed either by



Figs 34.2A and B: Internal carotid artery stenosis, arteriogram (A) the narrowing—arrow, (B) after correction

direct puncturing of the carotid or vertebral arteries in the neck percutaneously or by catheterization of these vessels. In the latter method, which is the preferred one, a catheter is introduced into one of the peripheral arteries such as the femoral or brachial and it is passed up into the root of the aorta and then selectively into the carotid or vertebral artery on either side. After positioning the catheter tip in the desired vessels, radio-opaque iodinated contrast agent is injected under pressure into the catheter and a rapid series of X-rays is taken while injecting the contrast agent.

This is time-consuming and invasive procedure with a definite risk of minor and major complications requires hospitalization of the patient.

Digital Subtraction Angiography

Digital subtraction angiography (DSA) is an advancement over the conventional cerebral angiography. In this procedure, the contrast agent is administered intravenously and a series of X-ray images are obtained which are digitized and subjected to computer subtraction for enhanced images of the blood vessels. This can be done as an outdoor procedure. Although the intravenous injection of contrast permits satisfactory visualization of the bigger vessels in the neck, for visualization of intracranial blood vessels it is far from satisfactory. For this purpose, selective intra-arterial contrast injection is still required.

Ventriculography

This procedure, once employed in the past, mainly for investigating intraventricular and posterior fossa tumors and hydrocephalus, has now been replaced by CT and MRI.

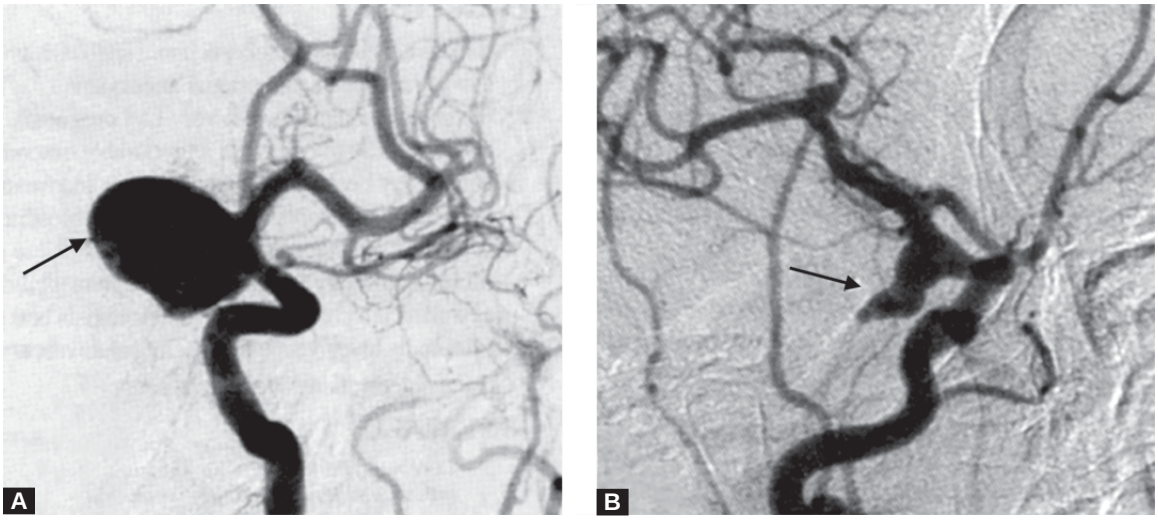
Pneumoencephalography

In pneumoencephalography (PEG) procedure, air is injected into the lumbar subarachnoid space and it is manipulated to enter the cerebral ventricles and subarachnoid space.

The air acts as contrast agent in X-ray studies. This procedure is invasive, and it is seldom done at present.

Myelography

This procedure which used to be carried out to investigate spinal cord lesions such as compression by extramedullary tumors or prolapsed intervertebral disks, intramedullary tumors and arachnoiditis is not done regularly at present. Since the introduction of



Figs 34.3 A and B: Carotid angiography. A and B show Berry aneurysm—arrows

CT and MRI, myelography is required only for a much smaller number of patients, greater information can be obtained by combining CT with myelography (CT-myelography).

Complications

Angiography, pneumoencephalography, ventriculography and myelography and associated with potential complications. Mild reactions include anaphylaxis, headache, vomiting, and convulsions. Serious reactions include, encephalopathy, worsening of neurological status, meningitis and death. Air embolism may complicate pneumoencephalography.

Radioiodinated Serum Albumin Cisternography

By injecting 99 technetium-tagged serum albumin into the lumbar subarachnoid space, its flow into the intracranial subarachnoid space and the ventricles is monitored and imaged sequentially over a period of time, to visualize its distribution. Radioiodinated serum albumin (RISA) cisternography was mainly performed in suspected cases of normal pressure hydrocephalus and CSF rhinorrhea. This is also replaced now by CT and MRI.

COMPUTED TOMOGRAPHIC SCAN

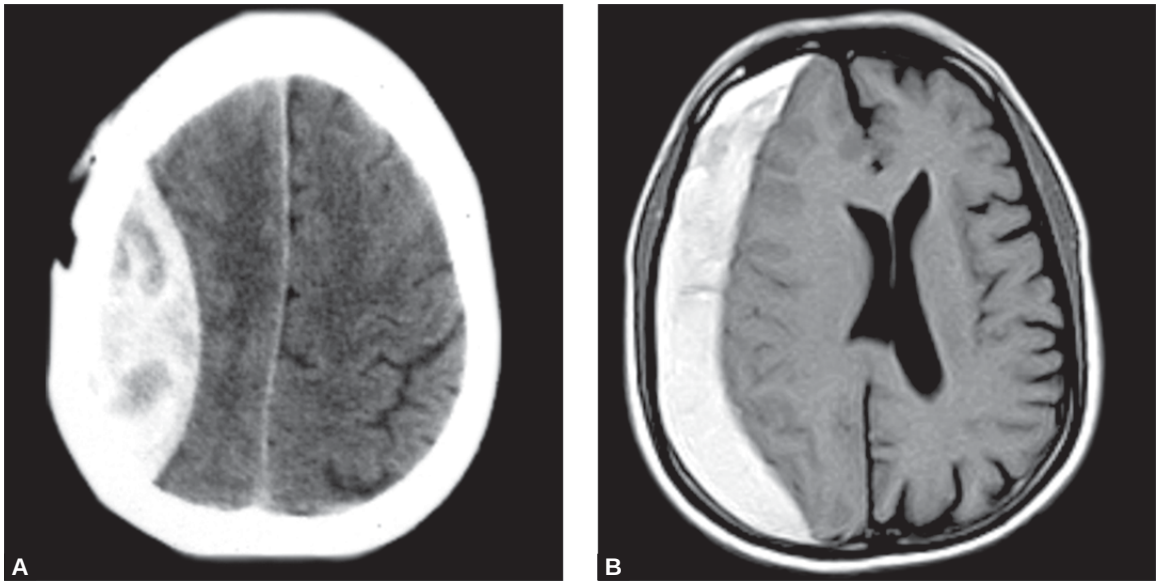
At present computed tomographic scan (CT) scan has become a part of routine investigations in the evaluation of many neurological problems. In most of the towns and cities in India CT scan centers have come up. The cost is relatively high, ranging from Rs. 1000 to Rs. 5000 depending upon the part imaged (Figs 34.4 to 34.6A).

Indications

The CT scan of the head is indicated and essential for diagnosis and management of the following conditions:

A patient with:

1. Focal neurological deficit of relatively recent onset and of undetermined cause, especially vascular accidents, hemorrhages, thrombosis or embolism.
2. Features of definite or suspected raised intracranial pressure
3. Altered sensorium or mental status of undetermined cause
4. Focal seizures of recent onset



Figs 34.4A and B: CT scan showing (A) extradural and (B) subdural hematomas. *Note:* The hematoma compressing the brain tissue and leading to pressure effects, i.e. distortion of the ventricles and shift of midline structures

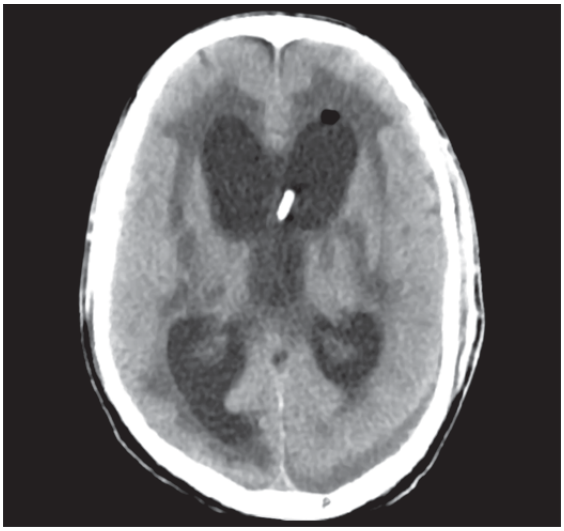


Fig. 34.5: CT scan showing hydrocephalus
Note: The dilated ventricles and thinned cortex

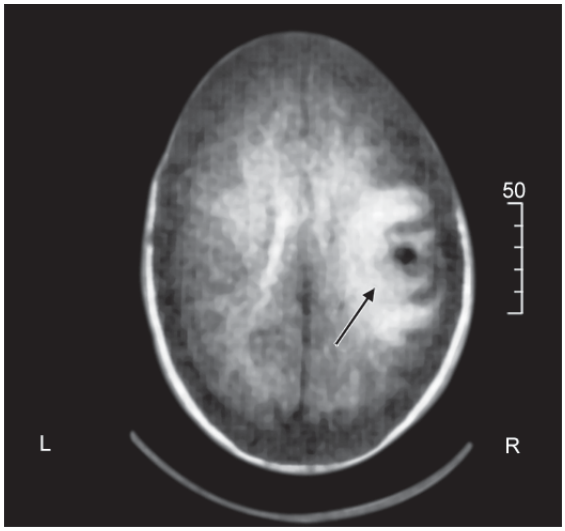


Fig. 34.6A: CT scan. Tuberculoma right parietal lobe (see arrow). Male aged 26 with epilepsy. Completely cleared with therapy

5. Late onset seizures
6. Subarachnoid hemorrhage
7. Head trauma
8. Suspected intracranial mass lesion
9. Parasitic diseases of the brain, e.g. hydatid cyst, cysticercosis.

CT scan is also the procedure of choice in patients in whom MRI is contraindicated due to the presence of implanted cardiac pacemakers, mechanical heart valves or magnetizable intracranial metal clips.

Although a normal CT is sometimes reassuring to the patient as well as to the clinician, the practice of ordering CT scan indiscriminately should be discouraged. Under no circumstances, CT should be considered as a substitute to clinical examination. *CT scanning delivers a high dose of irradiation which should be avoided if possible*

Limitations: While CT imaging of the supratentorial structures in the brain is quite good, its use in the evaluation of the posterior fossa structures such as brainstem and the cerebellum is limited because of the beam-hardening artifacts of adjacent bones. For the same reason, CT for the evaluation of spinal cord diseases is less than satisfactory. The other limitations of CT are its inability to reveal very small lesions, isodense lesions (lesion density same as that of normal brain) and cerebral infarcts in the first 24 to 48 hours of their occurrence. Hence, a normal CT does not ensure that all possible structural pathologies have been excluded. In such situations MRI may reveal abnormalities.

MAGNETIC RESONANCE IMAGING

Magnetic resonance imaging (MRI) offers better visualization of the anatomy of the brain and the spinal cord because of its high resolution. This is also a safe, rapid and noninvasive procedure like CT, but it is more expensive (Rs. 5000 to Rs. 12000 per study). The advantages of MRI over CT scan are (Figs 34.6B, 34.6C and 34.7):

1. It has better spatial and contrast resolution than CT
2. It is free of exposure to radiation
3. It is free of bone artifacts
4. Several additions studies of function, e.g. cardiac output, cornonary blood flow and metabolic activities can be performed by suitable modification.

For MRI scan, the patient has to be kept in a highly confined space which makes some patients claustrophobic, with modern machines the speed of imaging is more, so also the tendency for claustrophobia and discomfort is less.

MRI is the investigations of choice for lesions in the posterior fossa and spinal cord, such as syringomyelia and other structural lesions. Because of its higher resolution, it is also useful to detect



Fig. 34.6B: MRI showing periventricular lesions in MS. *Note:* The demyelinated plaques



Fig. 34.7: MRI cervical spine showing demyelinating lesions in a patient with transverse myelitis. *Note:* (1) general swelling of the cord and (2) hyperintense (whitish) lesions

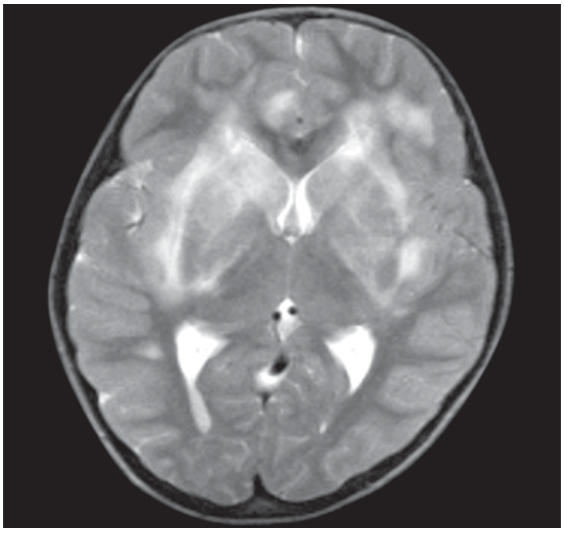


Fig. 34.6C: Showing white matter and basal ganglia lesions in ADEM

smaller lesions in the cerebral hemispheres such as demyelinating plaques in multiple sclerosis, small granulomas such as tuberculomas and cysticercosis cysts, which may escape detection on CT.

Developments in MRI

1. *Magnetic resonance angiography (MRA):* MR angiography is an effective, noninvasive tool to evaluate the vasculature. There is no need to inject any contrast material for MRA. The main types of imaging performed in MRA are time-of-flight (TOF), and phase-contrast (PC) angiograms. Both techniques allow the acquired data to be processed to generate images similar to those produced by conventional catheter angiography. MRA allows noninvasive assessment of neck vessels as well as large intracranial vessels. However, its disadvantages are its high cost, restricted availability, and inability to evaluate small intracranial vessels.
2. *Magnetic resonance spectroscopy (MRS):* Whereas MRI provides anatomical information based on signals from water in the tissues, MR spectroscopy provides chemical information on tissue metabolites. The atomic nuclei that can be studied by MR spectroscopy are H^{+1}, P^{31}, Cl^{13}, F^{19} and Na^{23}. This technique can provide useful information in the diagnosis of brain tumors, epilepsy, multiple sclerosis, Alzheimer's disease and various other degenerative diseases.
3. *Fluid attenuated inversion recovery (FLAIR):* FLAIR MRI sequence produces images in which parenchymal lesions give high signal and CSF gives a low signal intensity. This helps in the differential diagnosis of areas of high signal on T2-weighted images, by making the lesions more conspicuous.

4. *Functional MRI (FMRI):* Fast imaging methods, such as echoplanar imaging can provide images of working brain, almost in real time with a good resolution. Using this technique, it is possible to delineate areas of brain that are responsible for specific functions such as primary sensory and motor cortex, lateralization of language function and others. This is being employed to delineate the speech area during the neurosurgical procedures.
5. *Diffusion-weighted* (DW) *and perfusion-weighted* (PW) *MRI:* These are MR imaging techniques that are sensitive to the early pathophysiologic changes induced by cerebral ischemia (e.g. acute ischemic stroke). Soon after the onset of ischemic stroke, if MRI is performed using these techniques, it is possible to detect the extent of actual infarct on DW MRI and also the extent of the surrounding ischemic area (ischemic penumbra) on PW MRI . This information may guide the clinician for thrombolytic treatment in acute ischemic stroke.

POSITRON EMISSION TOMOGRAPHY

Whereas CT and MRI techniques provide information regarding the structural details of the brain and the spinal cord, positron emission tomography (PET) provides information about their function also.

It is performed by administering intravenously or by inhalation, a positron-emitting radio nucleide of very short half-life. This necessitates the availability of a cyclotron near the scanning site in order to provide the radio-isotopes. Because of this requirement, its cost is high (>Rs 15000). This investigation is available in a limited number of centers in India. The PET which used to be used mainly as a research tool has found its place increasingly in clinical work. The combination of PET and CT (PET-CT) is of great use in diagnozing and qualtifying malignancy and other lesions when other modalities are inconclusive. Processes such as cerebral blood flow, glucose and oxygen metabolism and cerebral blood volume can be studied noninvasively both in health and disease. The concentrations and locations of various neurotransmitters and their receptors can also be determined with PET. Combination of PET and CT (PET-CT) is being employed more frequently to get proper diagnosis of lesions which are not clearly diagnosed by CT or MRI.

SINGLE PHOTO EMISSION COMPUTED TOMOGRAPHY

Like PET, single photo emission computed tomography (SPECT) also provides information about the function of the brain. It also involves administration of gamma ray emitting radionucleides. However, these radionucleides are of longer half life and hence do not need a costly cyclotron near by. Therefore, SPECT can be described as a poor man's PET. It is now available only in some centres for clinical use, especially to study cerebral blood flow, cerebral blood volume and cerebral neurotransmitter receptors.

ECHOENCEPHALOGRAPHY

This noninvasive ultrasound investigation, which was popular before the advent of CT scanner is still useful to detect the shift of the midline structures caused by supratentorial space occupying lesions, and to detect the size of the ventricles. Currently, an advanced real time ultrasound scanner capable of high resolution is available to diagnose intracranial hemorrhage in infants.

IMAGING STUDIES OF MUSCLES

Although imaging studies of skeletal muscles are not routinely performed, ultrasound, CT, and MRI can quantify muscle atrophy, identify the muscle groups that are affected, detect fibrofatty tissue replacement in the muscles, and locate muscle and tendon abscesses and other pathologies in the muscles and tendons. Technetium diphosphonate or pyrophosphate imaging can demonstrate muscle fiber damage in polymyositis.

DUPLEX DOPPLER SCANNER

Doppler ultrasound which is a noninvasive investigation employed to study the arterial wall and the blood flow within the extracranial portion of the carotid arteries, is useful to detect carotid stenosis and occlusions.

Transcranial Doppler Ultrasound

This is a noninvasive procedure which provides useful information about cerebral blood flow velocity. Using a low frequency (2MHz) ultrasound, it is possible to study blood flow velocity in the proximal parts of middle, anterior and posterior cerebral arteries, terminal part of internal carotid artery and intracranial vertebrobasilar system. It is useful in detecting intracranial arterial stenosis, vasospasm, cerebral emboli and cerebrovascular hemodynamic reserve.

HISTOPATHOLOGICAL STUDIES

Brain Biopsy

Brain biopsy as a diagnostic method, though available for many years, is sparingly undertaken at present with the introduction of advanced neuroradiological and neurophysiological techniques.

In the majority of cases, this procedure is undertaken by neurosurgeons. With the availability of stereotaxic frames, stereotaxic brain biopsy of very localized and small lesions can be performed with precision and safety.

The indications for brain biopsy are:

i. Focal intracranial lesions
ii. Chronic, progressive cerebral disorders of diffuse character accompanied by mental retardation or dementia, in whom all other possible diagnostic methods have already been done, but have failed to provide sufficient diagnostic certainly.

Brain biopsy should be undertaken only when laboratory facilities and staff experienced in the interpretation of the biopsy material are available.

Muscle and Nerve Biopsy

These biopsy procedures should be carried out by experienced persons because any damage to the tissue during biopsy will seriously hamper the correct interpretation by the pathologist.

Muscle biopsy is of value in the diagnosis of congenital myopathies, storage diseases of the muscle, vasculitis and polymyositis. It is also helpful in differentiating long-standing muscle weakness and wasting due to a primary muscle disease from neurogenic atrophy, when clinical and electrophysiological features are equivocal.

Nerve biopsy is useful to differentiate axonal from demyelinating neuropathies. Hereditary hypertrophic neuropathies, infective neuropathies like leprosy and infiltrative neuropathies such as sarcoidosis and amyloidosis and vasculitis, can also be identified by nerve biopsy.

The field of neurological studies and investigations are proceeding at a fast pace and newer and newer tests are being added on.

PART–II
Specialties

SECTION

12

Pediatrics

CHAPTER

35 Clinical Examination of Children

KE Elizabeth

Case recording format, Physical examination, Hand to head to foot examination, Assessment of growth (Anthropometry), Nutrition, Trivandrum development screening chart, Investigations, New born baby

INTRODUCTION

Clinical examination in infants and children is an art that clinicians have to master. Unlike in adults, a unique format has to be followed in pediatrics. It is important to record about the informant, about antenatal, natal and neonatal events that may be contributory to the diagnosis. Dietary history starting from breastfeeding, complementary feeding, present diet, developmental mile stones, immunization history, family history including parents, sibling and pedigree charting, socioeconomic background, housing conditions are to be recorded using the format given below.

Terminologies for different stages of growth

0–28 days:	Neonate
0–12 months:	Infant
1–3 years:	Toddler
3–6 years:	Preschool child
0–5 years:	Under five child
10–19 years:	Adolescence period

CASE RECORDING FORMAT

History

1. *Sociodemographic/Personal Data*
 - Name
 - Age in years and months (date of birth when relevant)
 - Gender
 - Address, geographic location
 - Informant and reliability of the history.
2. *Presenting Complaints*
 - List chief complaints in chronological order.
3. *History of Present Illness*
 - Mode of onset, duration, and progression
 - Associated symptoms, aggravating and relieving factors
 - Points relevant in etiology, complications and negatives points
 - Treatment history, course of the illness, etc.
4. *History of Past Illness*
 - Similar illness
 - Episodes of common childhood illnesses like acute respiratory infection (ARI), acute diarrheal disease (ADD), vaccine preventable diseases (VPDs), febrile fit, previous hospitalizations, etc.
5. *Antenatal History*
 - Antenatal care, AN visits, Inj. tetanus toxoid, iron and folic acid (IFA) tablets, ultrasound scan reports, anomaly scan, exposure to exanthematous fevers, drugs, radiation, addictions, systemic diseases, and pregnancy related illnesses.
6. *Natal History*
 - Gestational age, birth weight
 - Mode and place of delivery, birth cry
 - Initiation of breastfeeding,
 - Resuscitation, neonatal intensive care unit (NICU), medications/procedures like umbilical cannulation.

7. *Neonatal History*
 - Hospital stay, special care
 - Jaundice, cyanosis, fits
 - Feeding practices.
8. *Developmental History*
 - Gross motor, fine motor adaptive, language, personal social milestones vision, hearing.
9. *Dietary History* including Infant and Young Child Feeding (IYCF) Practices.
 - Enquire about the following:

Breastfeeding History

Complementary feeding, empowering to take all what is cooked at home at one year of age (family pot feeding), cooking practices, diet during illness, any exclusion diet, food fads, adequacy of calories, protein and micronutrients, supplementary feeding.

BEDSIDE CALCULATIONS AND NORMOGRAMS

Bedside Calculation of Energy

The minimum energy requirement of a child can be calculated using the following formula:

– 1year –1000 Kcal
– 1–9 years –1000 + 100 Kcal for each completed year.
– Adolescent Boy–2400
– Adolescent Girl–2200
– ICMR recommendations of recommended dietary allowances (RDA). (2009)

Age	0–6 m (g /Kg)	6–12 m (g/Kg)	1–3 yr g	4–6 yr g	7–9 yr g	10–12 yr g
Protein	1.16	1.69	15.7	20.3	29.6	39.9 boys, 40.4 girls

– Bedside recommended dietary allowances of vitamins and minerals
 - A-1500 IU
 - D-400 IU
 - E-5–15 IU/kg
 - C-40 mg
 - B_1 = 0.5 – 1.5 mg
 - B_2 = 0.5 – 1.5 mg
 - B_3 = 5 – 15 mg
 - B_6 = 0.5 – 1.5 mg
 - Folic acid-10–150 mcg
 - B_{12}-0.5–1.5 mcg
 - Calcium = 500–1000 mg
 - Phosphorus-800–1000 mg
 - Magnesium-200–300 mg
 - Iron-10–20 mg
 - Iodine-50–150 mcg
 - Copper-1–2 mg
 - Zinc-5–15 mg
 - Fluoride-1–5 mg
 - Manganese-1–5 mg
 - Selenium-100 mcg
 - Chromium-10 mcg
– Immunization History
 - Whether fully immunized for age as per Universal Immunization Program (UIP) or Indian Academy of Pediatrics (IAP) schedule.
 - BCG Scar, the last vaccine the child has received and the next vaccine that is due (Table 35.1).
 - IAP immunization time table (revised in 2008)

Table 35.1: Vaccination schedule

Age	*Vaccine*	*Route*
	BCG	Intradermal
Birth	OPVo	Oral
	Hepatitis B_1	Intramuscular
	$DTPw_1/DTPa_1$	IM
	$OPV_{1* + IPV\ 1}$	ORAL
6 weeks	Hepatitis B_2	IM
	HIB_1	IM
	$DTPw_2/DTPa_2$	IM
	$OPV_{2 + IPV\ 2}$	ORAL
10 weeks	HIB_2	IM
	$DTPw_3/DTPa_3$	IM
	$OPV_{3 + IPV\ 3}$	ORAL
14 weeks	Hepatitis B_{3**}	IM
	HIB_3	IM
9 months	Measles	Subcutaneous
15–18 months	$DTPwB_1/DTPA\ B_1$	IM
	OPV 4	ORAL
	HIB B_1	IM
	MMR1	Subcutaneous
2 years	Typhoid #	IM
	DTPw B_2/DTPa B_2	IM
5 years	OPV5, MMR 2 $	ORAL
10 years	Td/ Tdap/TT, HPV ^	IM
16 years	Td/ Tdap/TT	IM

* OPV alone if IPV cannot be given
** 3rd dose of Hepatitis B can be given at 6 months of age, HBV given at birth may also be considered as zero dose and 3 doses can be given along DTP 1, 2 and 3
Revaccination every 3 years
^ In females 3 doses at 0, 1 and 6 months

Pregnant women – 2 doses of TT at monthly interval

Vaccines that have to be Given After Discussion with Parents

Age	*Vaccine*	*Route*
> 15 months of age	Varicella Vaccine#	SC
> 18 months of age	Hepatitis A vaccine ^	IM
> 6 weeks of age	*rotavirus, pneumococcal conjugate vaccine (PCV7)	IM

< 13 years of age: 1 dose; > 13 years of age: 2 doses at 4 to 8 weeks interval

^ 2 doses at 6 to 12 months interval

* Rotavirus vaccine—2 to 3 doses as per brand at 4 to 8 week interval 6 week to 6 month old

PCV 7 to 3 primary doses at 6, 10 and 14 weeks followed by a booster at 15 to 18 months.

IMMUNIZATION IN SPECIAL CIRCUMSTANCES

1. *Immunization in preterm infants:* In general, all vaccines may be administered as per schedule to stable babies, according to the chronological age, irrespective of birth weight or period of gestation. Very low birth weight/preterm babies can be given immuni zations after initial stabilization. HBV is usually given when baby attains 2 kg weight.
2. *Children receiving corticosteroids*: Children receiving oral corticosteroids in high doses (e.g. Prednisolone 1 to 2 mg/kg/day) for more than 14 days should not receive live virus vaccines until the steroid has been discontinued for at least one month. Killed vaccines are safe but may be incompletely effective in such situations. Patients on topical or inhaled steroid therapy should not be denied their age appropriate vaccines.
3. *Children awaiting splenectomy*: Children with loss of splenic function are at high risk of serious infections with encapsulated organisms. If surgical splenectomy is being planned, immunization with pneuumococcal, HIB and meningococcal vaccines should be initiated a few weeks prior to splenectomy.
4. *Vaccination in children with HIV infection*: Children infected by HIV are particularly vulnerable to severe, recurrent, or unusual infections by vaccine preventable pathogens. It must be emphasized that routine immunizations seem to be generally safe in such children, but the immune response following vaccination would depend upon the degree of immunodeficiency at that point of time. Immune attrition associated with viral replication may particularly interfere with memory responses. Consideration should be given to readministering childhood immunizations to such children when their immune status has improved following antiretroviral therapy.

Vaccination Schedule for Adolescents

No.	*Vaccine*	*Age*
1.	Td/TT	Booster at 10 and 16 years
2.	MMR vaccine	One dose if not given earlier
3.	Hepatitis B	Three doses (20 mcg) 0, 1 and 6 months if not given earlier
4.	Typhoid vaccine	Vi Polysaccharide vaccine every three years
5.	Varicella vaccine*	One dose up to 13 years and 2 doses (at 4 to 8 weeks interval) after 13 years of age if not given earlier
6.	Hepatitis A vaccine*	Two doses 0 and 6 months if not given earlier.
7.	Human papilloma virus vaccine (for girls).	Three doses 0, 1 or 2 months, 6 months starting at 10 years of age.

*Only after discussing with parents on a one to one basis

Family History

- Consanguinity, construct a three-generation pedigree in genetic disorders
- Age and health of parents
- Family planning measures adopted
- Details of siblings, unexplained deaths in the family
- Contact with TB, history of diabetes, allergic disorders, and similar illness in the family.

Socio-economic History

Record socioeconomic status, occupation, education and family income, any insurance or financial reimbursement/ESI benefits.

Also record housing conditions, sanitary facilities, source of drinking water, pets and recent travel.

PHYSICAL EXAMINATION

A. General Examination
 1. General comment: Appearance, well-being, attitude, hydration, color, sensorium
 2. Vital signs (Table 35.2)

a. *Temperature:* Keep the thermometer *in-situ* for 1 to 2 minutes before taking the reading. Oral, axillary, rectal, ear drum or skin temperature can be measured. In newborns, rectal or axillary temperatures are measured. Low reading thermometers which can record as low as 30°C, may be needed to detect hypothermia. In young children axillary temperature and in older children and adults, oral temperature is measured. Normal core temperature is 37°C or 98.6°F. Skin temperature is 1°C lower than core temperature. Hyperpyrexia is >41°C (105°F) and hypothermia <35°C(95°F). For axillary reading, 0.5°C or 1°F is added to get the core temperature except in newborn babies, who have relatively more of metabolically active brown fat in the axilla.

Fever is accompanied by tachycardia, 18 beats/1°C or 10 beats/1°F. Extremities may be cold in a febrile child due to vasoconstriction and there may be associated chills and rigor. Children are more prone to develop febrile convulsions.

b. *Respiration:* Record rate, rhythm, type, work of breathing, retractions, accessory muscles. (Rate to be counted for 1 minute when the child is settled and quiet, by observing breathing and not by palpation)

c. *Pulse:* Record rate, rhythm, volume, character. (Start feeling radial pulse and count for 1 minute, except in emergency, when it may be counted for 6 seconds and multiplied by 10), subsequently feel for all peripheral pulses. Carotid, femoral, brachial and axillary pulses are also to be palpated if peripheral pulses are not well felt. Compare between radial and dorsalis pedis; if dorsalis pedis is weak, feel for femorals and look for radiofemoral delay in suspected coarctation of aorta. Heart rate and pulse rate may vary in arrhythmias and in ectopic beats, In atrial fibrillation, the difference between PR and HR will be >10.

d. *Blood Pressure:* Use appropriate BP cuff size—in order to cover middle 3rd of the upper arm. Smaller cuff will give higher BP. BP cuff sizes are given below:

- 3.5 cm,
- 7 cm or
- 12.5 cm (standard) Both palpatory and auscultatory methods are used.

50th centile of BP is roughly 90 + (2 X) and 5th centile is 70 + (2X), where 'X' is age in years.

The average BP of newborn is 60/40, which is half of the adult BP and at 1 year, it is 90/60 mm of Hg.

Other methods of recording BP are oscillometric, doppler and intra-arterial techniques. Noninvasive BP (NIBP) recording is done in ICUs.

e. *Capillary filling Time (CFT):* Raise the limb above the heart level and press the pulp of the finger or sole of the foot, observe the time taken for capillary filling by the disappearance of the blanch. Usually it is 2 seconds. Three or more seconds is abnormal. Exposure to cold may lead to prolonged filling time especially in the newborn.

Table 35.2: Vital signs as per age

Age	*Respiratory rate*/ mt (Usual rate)*	*Heart rate** /mt. or pulse rate (Usual rate)*	*Systolic BP*** mm of Hg (Systolic/Diastolic)*
New born	30–60 (40)	90–180 (140)	50–70(60/40)***
6 mths	24–40	85–170	65–106
1 Yrs	20–40 (30)	80–140 (120)	72–140 (70/50)
3 Yrs	20–30	80–130	78–114
6 Yrs	18–25 (20)	70–110 (100)	80–116 (90/50)
8 Yrs	18–25	70–110	84–122
10 Yrs	16–20	65–110 (90)	90–130 (100/70)
12 Yrs	14–20 (18)	60–110 (80)	94–136 110/80

*RR-Fast Breathing: Newborn- > 60, Infant > 50, Under five > 40, Older > 30, Adult > 20

**HR – Abnormal: Newborn- < 100 and >200, Young child < 80 > 180, Older child < 60 and >160

***BP- Normal: 90 + (Age in yrs X 2), Lower Limit: 70 + (Age in yrs X 2)

****Diastolic BP is 2/3rd of Systolic BP

- Resp. and Heart rates of Newborn are double that of adult and BP is half that of the adult.
- Adult: RR - 18–20, HR-70 and BP-120/80

Sensorium

- Alertness - AVPU Scale
 - **A:** Awake/alert
 - **V:** Verbal response present
 - **P:** Pain response present
 - **U:** Unresponsive/unconscious
- ***Glasgow coma scale (GCS):*** This scale is commonly employed to evaluate the degree of comma resulting from head trauma or cardiorespiratory arrest. It correlates well with prognosis for recovery and also helps to plan emergency management. In coma due to many medical conditions, its application and correlation with prognosis is less clear. The parameters taken into considerations are openings of the eye, best verbal or gesture response and best motor response. The response is graded from 1 to 6 and the total score is determined. Higher scores are indicative of better outcome.

Eye Opening

- None
- To pain
- To speech
- Spontaneous.

Best Verbal Response for Adults

- None
- Incomprehensible sounds
- Inappropriate words
- Confused
- Oriented.

For Infants and Toddlers

- None
- Restless, agitated
- Persistently irritable
- Consolable cry
- Appropriate words, smiles, fixes and follows.

Best Motor Response

- None
- Extensor response
- Abnormal flexion
- Withdrawal
- Localizes
- Obeys.

Score: 13 to 15 mild, 9 to 12 moderate and <8 is severe coma

HAND TO HEAD–TO-FOOT EXAMINATION

Start with examination of the hands in order not to forget looking at hands.

1. Record "PICCLE"

Pallor	Clubbing
Icterus	Lymphadenopathy
Cyanosis	Edema

2. Hand: Look for poly/syndactyly, radial ray anomalies, absent radius, clinodactyly, Simian crease (Fig. 35.1), dermatoglyphics, polydactyly on the side of the thumb is preaxial/radial polydactyly, on the side of little finger is postaxial/ulnar polydactyly, in between is called mesoaxial polydactyly.
3. Head:
 - Look for frontal, parietal and occipital prominence
 - Plagiocephaly is localized flattening of bones
 - Shape of scalp, forehead bulging, prominent veins
 - *Sutures:* Metopic suture is noted in the midline of forehead. Palpable sutures, ridging of sutures like 'Keel of the ship' is seen in craniostenosis and overriding sutures with step formation is seen in microcephaly due to reduced brain growth.
 - Fontanels—depressed/bulging, open/closed, pulsatile, borders felt/not, measure the size also.

Fontanel is the meeting point of 3 bones. At birth there are 6 fontanels, anterior (AF) at the meeting point of frontal and 2 parietal bones, posterior (PF) at the meeting point of occipital and 2 parietal bones,

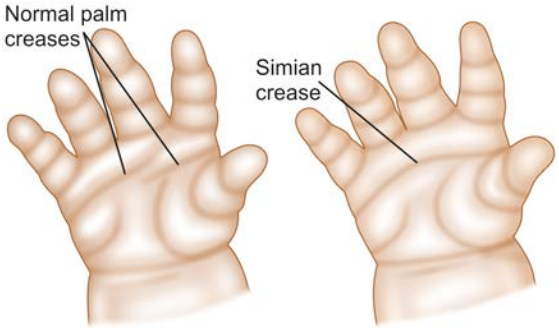


Fig. 35.1: Palmar creases in normal and down syndrome (simian crease)

anterior lateral (ALF) at the meeting point of frontal, parietal and temporal on either side and posterior lateral (PLF) at the meeting point of occipital, parietal and temporal bones on either side.

AF closes by 9 months—1½ yrs, PF by 3 to 6 months, Usually PF is not palpable at birth and if posterior fontanel is open and palpable at birth, check for hypothyroidism, hydrocephalus or skeletal dysplasia.

Bones may be brittle and ping pong sensation or egg shell crack may be elicitable in preterms and in rickets.

Hair

Look for color, pigmentation growth, texture, hair lines, sparse hair, pluckability and seborrhic dermatitis (cradle cap).

Face

Look for dysmorphism, mooning of face, coarse facies, midfacial hypoplasia, micrognathia/retrognathia, thick or thin lips, long philtrum and features of the maxilla.

Eyes: Look for

- Position and slant: >10% – upward or downward slant
- Pallor, icterus, blue sclera, Vitamin deficiency.
- Hypertelorism, conjunctival congestion, microphthalmia, corneal clouding, coloboma, cataract, nystagmus
- strabismus, muddy cornea

Synorphis is meeting of eyebrows in the midline.

Ears: Look for

- Deformities, Preauricular tag/sinuses, discharge
- Ear position: Normally one-third of the pinna is above the inner canthus of the eye, if it is <10% of the pinna, low set ear is diagnosed.

Nose

Look for flat nasal bridge, upturned position, deviation of nasal septum (DNS).

Tongue

Look for the color of the tongue and its surface

- Glossitis—color of tongue is red or magenta with desquamation.
- Thrush.

Tongue is protruded in cretinism, down syndrome and angioneurotic edema.

Mouth: Look for

- Oral hygiene, dental caries, throat /tonsil
- Cleft lip/palate, vitamin deficiency
- Color and no. of teeth,
- Inverted V-shaped upper lip seen in myopathy.

Neck: Look for

- Length of the neck (distance between external occipital protuberance and C_7 spine)

Normally the fraction $\frac{\text{height}}{\text{length of the neck}}$ is > 13.7. Values <13 indicate 'short neck' which is suggestive of craniovertebral anomalies.

- Look for webbing of the neck and, low hair line,
- Thyroid and lymph node enlargement, pulsations.

Chest: Look for

- Sternum—pectus excavatum (depression) seen in upper airway obstruction, Marfan's syndrome and in some cases of rickets pectus carinatum (bulging) seen in rickets, skeletal dysplasia, long standing heart diseases
- Absent pectoralis major (Poland syndrome)
- Wide spaced nipple, absence of nipple (athelia) or accessory nipples (polythelia).
- Normally the distance between nipples is less than one-third of the chest circumference
- Look for shield chest, precordial bulge, barrel shaped chest
- Harrison's sulcus/groove is depression along the attachment of the diaphragm from sternum to mid axillary line in the lower chest wall. It is seen in rickets. It may also be due to chronic heart failure, chronic wheeze from infancy, congenital laryngeal stridor, cystic fibrosis, myopathy, spinal muscular atrophy or a congenital anomaly.

Abdomen: Look for

- Umbilical hernia
- Dilated veins
- Divarication of recti
- Distension
- Ascites
- Hernial orifices

Genitals: Look for

- Ambiguous genitalia
- Undescended testis

- Precocious puberty
- Hydrocoele, scrotal edema
- Micropenis/macropenis macro-orchidism in fragile X syndrome is may be evident during and after puberty.

Upper Limbs: Look for

Palms: Look for

- Simian crease
- *poly/syndactyly* adherent fingers, *arachno dactyly* long spider like fingers (Marfan's), *clinodactyly* (permanent flexion of fingers and toes), *camptodactyly* (permanent medial or lateral deviation of one or more fingers)
- Short limbs, board thumbs, cyanosis, clubbing palmar erythema, flap, pallor, dermatoglyphics
- Koilonychia (spoon shaped nails), white nails dystrophic nails and others
- Capillary filling time indicative of the micro circulation.

Lower Limbs: Look for

- Hyper mobility
- Joint swelling – knee, ankle
- Deformities, weakness
- Congenital talipes equino varus (CTEV)
- Chappal sign (Sandal gap) between big toe and 2nd toe in trisomy 21
- Kennedy sulcus (a crease seen on the sole starting between the big toe and the second toe and extending proximally) suggestive of down syndrome
- Rocker bottom feet (Trisomy 18)
- Pedal edema,
- Arches of feet.

Spine: Look for

- Dimples, hairy patches, cleft, open/occult meningo myelocele
- Gibbus-swelling
- Kyphosis, scoliosis, lordosis.

Skin: Look for

- Neurocutaneous markers, nevus
- Pyoderma scars, scabies
- S/C emphysema, skin turgor
- Phrynoderma
- Rashes.

Congenital anomalies: Search carefully for congenital anomalies.

ASSESSMENT OF GROWTH (ANTHROPOMETRY)

Auxology is the preferred term for human live measurements. Anthropometry is comparison with reference standards or normal range. Interpretation of anthropometry, whether normal or otherwise and assessment of the grade of malnutrition. (Stunting Table 35.3, wasting, obesity, microcephaly and others)

- Bedside calculation: Bedside calculation for weight*, height**, head circumference

 **Add 2 kg/year in 1 to 6 years of age and add 3 kg/year thereafter till puberty.*

 ***Add 6 cm/year after 2 years of age till puberty.*

Weight doubles by four months and triples by twelve months. The height doubles by four years and triples by twelve years.

- Weech's formula for calculation of weight

 At birth 3 Kg

 3–12 m $\frac{\text{age in months} + 9}{2}$

 1–6 yrs $2 \times \text{age in years} + 8$

 7 – 12 yrs $\frac{7 \times \text{age in years} - 5}{2}$

Table 35.3: Anthropometric measurements as per age

Age (years)	*Weight (kg)*	*Height (cm)*	*Head circumference (cm)*
Birth	3	50	33–35
3/12	5	60	39–40
6/12	7	66	42–44
9/12	9	71	44–45
1	10	75	45–47
2	12	87	47–49
3	14	94	49–50
4	16	100	50–51
5	18	106	50–52
6	20	112	51–52
7	23	118	
8	26	124	
9	29	130	
10	32	136	
11	35	142	
12	38	150	

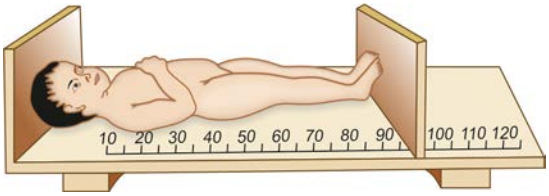


Fig. 35.2: Infantometer

IAP classification of protein energy malnutrition (PEM) (Weight for age)

71–80%	Gr.I PEM
61–70%	Gr.II PEM
51–60%	Gr.III PEM
< 50%	Gr.IV PEM

Add K to the grade to indicate Kwashiorkor According to Wellcome Trust clinical classification weight 60 to 80% of the expected with edema is kwashiorkor and without edema is undernutrition and weight <60% of the expected with edema is marasmic kwashiorkor and without edema is marasmus.

Height

(Doubles by 4 yrs and triples by 12 yrs) For measuring height <2 years – use the i*nfantometer* (Fig. 35.2). For older children use the *stadiometer* or *anthrometric* rod. Recumbent length is 1 cm more than standing height. Height of infants and childern as per age is listed in Table 35.4.

Table 35.4: Height of infants and children as per age

Birth	6 mo	1 yr	2 yr	4 yr	8 yr	12 yr
50 cm	66 cm	75 cm	87 cm	100 cm	125 cm	150 cm

- The adult height is generally twice the height attained at two years (2 × height at 2 yr = adult height)
- Weech's formula for height of children aged 2 to 12 years is given below
- Height in cms = (6 × age in years) + 77

Waterlow classificaion for stunting (height for age) indicating chronic malnutrition is listed in Table 35.5.

Table 35.5: Waterlow Classification for stunting (Height for age)

Height for age	*Grade of stunting*
Normal	> 95%
I degree	90–95%
II degree	85–89%
III degree	< 85%

Waterlow classification for wasting (weight for height) indicating acute malnutrition is listed in Table 35.6.

Table 35.6: Waterlow Classification for wasting (Weight for Height)

Weight for height	*Grade of wasting*
> 110%	overweight
91–110%	normal
81–90%	I degree wasting
70–80%	II degree wasting
<70%	III degree wasting

NUTRITION

WHO Classifications

1. WHO grading and interpretation
 - Normal weight, normal height, normal W for H- ***Normal nutrition***
 - Decreased W, normal height, decreased W for H - ***A/C malnutrition***
 - Decreased W, decreased H, normal W for H - ***C/C malnutrition***
 - Decreased W, decreased H, decreased W for H - ***A/C on C/C malnutrition.***
2. WHO Classification of undernutrition is described in Table 35.7

Table 35.7: Features of undernutrition

Features	*Moderate*	*Severe*
1. Edema	No	Yes
2. Weight for Height (Wasting)	70–79 %	< 70%
3. Height for Age (Stunting)	85–89 %	<85%

Upper Segment (US): Lower Segment (LS) Ratio

Upper Segment is the distance between the upper margin of the pubic symphysis to the vertex (It is the total height – lower segment) - Height -LS.

LS distance between the upper margin of the symphysis pubic to toes.

Table 35.8 gives the US by LS ratios at different ages

Table 35.8: US/LS ratios

Birth	6 months	1 yr	2 yr	3 yr	4 yr
1.7:1	1.6:1	1.5:1	1.4:1	1.3:1	1.2:1

The US is shorter (short trunk) in spondylo epiphyseal dysplasia, kyphoscoliosis, mucopolysa ccharidoses and others.

The US is longer (short limbs) in achondroplasia, rickets (bow/legs), hypothyroidism and others.

Head Circumference (HC)

Maximum occipitofrontal circumference (OFC): The measurement is done at the following level:
Anteriorly–point above glabella
Posteriorly-occipital protuberance.

1. **Bedside Calculation:** ***DINE'S formula-*** Head circumference in cm in infant

$$= \frac{\text{length} + 9.5 \pm 2.5}{2}$$

In general, the head circumference increases two cm every month during the first three months, one cm/month for the next three months and there after 0.5 cm/month for six months (Table 35.9).

Chest Circumference (CC)

- Should be measured at the level of substernal notch in mid inspiration
- Infancy HC >CC, 1 yr HC = CC, > 1 year- CC >HC
- In Protein Energy Malnutrition (PEM) the ratio of HC : CC is more than 1 at 1 yr of age.

Midarm Circumference (MAC)

- Taken in children aged 1 to 5 yrs
- The left arm (triceps) is measured midway between acromion and olecranon process with the arm hanging freely by the side (Fig. 35.3).
 - Normal 13.5 cms
 - Moderate PEM 12.5 to 13.5 cms
 - severe PEM 12.5 cms or less.
- ***Skeletal maturation:*** In full term newborn babies, five ossification centers are present namely lower end of the femur and the upper end of the tibia in the knee and 3 tarsal bones namely talus, calcaneus and cuboid in the ankle. The head of the humerus is present by 1 month of age and the head of femur by 4 to 6 months. By 6 months, two carpal bones, capitate and hamate appear. At birth, these are cartilaginous bones. The eighth carpal bone-pisiform appears by 9 to 10 years (9 in girls and 12 in boys). Except for the first two, there is high variability in the appearance of the other carpal bones. The ossification centers appear first on the left side of the body and then on the right side and in girls first and later in boys.

 Mnemonic for 8 Carpal bones: 'Please Take Lovely Susan To The Coffee House'— Pisiform (last to appear, 9–10 years 9 in girls and 12 years in boys), Triquetral (3rd year), Lunate (4th year), Scaphoid, Trapezium, Trapezoid (these 3 by 4th year in girls & 5th year in boys), Capitate (2nd month onwards) and Hamate (3rd month onwards).

 Lower end of radius appears by 9 months and lower end of ulna by 6th year. These ossification centers are useful in assessing the bone age of the child. The bone age is delayed in hypopituitarism, hypothyroidism, severe malnutrition and maturational/constitutional delay. It is advanced in precocious puberty. Fusion of capitulum with the shaft at elbow predicts puberty within a year. Bone age is assessed by comparing with references.
- Dentition and enamel formation (Tables 35.10 to 35.13)
 - Young child: Number of milk teeth = Age in months – 6
 - Primary / Milk teeth are 20 in number. All of them erupt by 2½ years.

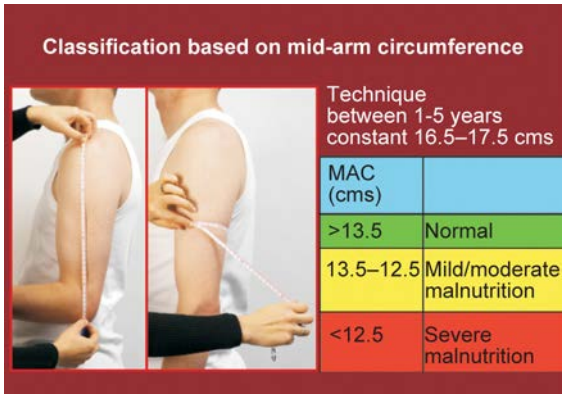


Fig. 35.3: Measuring mid-arm circumference

Table 35.9: Head circumference at different ages

Age	*HC*	*Age*	*HC*
Birth	35 cm	3 m	40 cm
6 m	43 cm	9 m	45 cm
1 yr	47 cm	2 yrs	49 cm
3 yrs	50 cm	4 yrs	50.4 cm
5 yrs	50.5 cm	9 yrs	52 cm

Note: A difference of >3.75 cm above or below the normal indicate macro-or microcephaly one standard deviation (SD) is 1.25 cm. Variation of 3 SD is abnormal.

Table 35.10: Eruption sequence of milk teeth

• Central incisors	6 – 7 months
• Lateral incisors	8 – 9 months
• Canine	16 – 18 months
• First molar	12 – 14 months
• Second molar	20 – 24 months

Table 35.11: Completion of enamel formation

• Central incisors	1½ months
• Lateral incisors	2 ½ months
• Canine	9 months
• First molar	6 months
• Second molar	11 months

Table 35.12: Permanent teeth eruption

• Central incisors	7 – 8 years
• Lateral incisors	8 – 9 years
• Canine	11 – 12 years
• First premolar	10 – 11 years
• Second premolar	10 – 12 years
• First molar	6 – 7 years
• Second molar	12 – 13 years
• Third molar	17 years +

Table 35.13: Permanent teeth enamel formation

Central incisors	4 – 5 years
Lateral incisors	4 – 5 years
Canine	6 – 7 years
First premolar	5 – 6 years
Second premolar	6 – 7 years
First molar	2 ½ – 3 ½ years
Second molar	7 – 8 years

Growth Charts and Growth Assessment

Growth charts were popularized by David Morley. These are used for growth monitoring. Well baby clinics, primary health centers and ICDS (Integrated Child Development Services) Scheme program utilize growth charts. The weight measurements of a child over a period of time are plotted on the growth chart and any deviation from the normal pattern can be visualized and interpreted. An upward curve in the 'road to Health' is ideal. In a child with normal nutritional status, the curve is within the 'road to health'. In a colored chart, this is the green zone. The curve of those with severe malnutrition will fall in the lower red zone and that for those with mild and moderate malnutrition will fall in the blue and yellow zones. A flat curve and a downward curve are not desirable. Such children should be investigated and followed up. They must also be given food supplementation.

Table 35.14: Growth velocity in the various age groups

• 0–6 months	15 cm
• 6 –12 months	7 cm
• 1st year	25 cm
• 1–2 years	10–12.5 cm/year
• 2–5 years	5–6 cm/year
• 5–12 years	5–6 cm/year

Growth Velocity (Table 35.14)

Weight gain or height gain over a unit period of time is velocity and it is a better indicator of growth. It reflects the effectiveness of any intervention namely nutritional supplementation, stimulation, growth hormone therapy and others. Weight velocity is 6 kg in the first year. In preschool child, it is 2 kg/year and in a school child, it is 3 kg/year till puberty. Height velocity is 25 cm in the first year, it is 12.5 cm in the second year and thereafter it is 6 cm/year till puberty (Fig. 35.4).

PHYSICAL EXAMINATION OF THE ADOLESCENT

Adolescence is the period between 10 to 18 years in girls and 11 to 20 years in boys. WHO considers 10 to 19 years as the period of adolescence for practical purposes. Sign of puberty before 8 years in girls and 9 years in boys is considered *precocious puberty*. Puberty/Adolescence is divided into *prepuberty, puberty and postpuberty or early, mid and late adolescence.*

Tanner's Sexual Maturity Rating (SMR) scale is used to stage puberty. Increased height velocity is an important event during puberty in both boys and girls.

In SMR scale, the stages are categorized into 1 to 5. The SMR picture scale that demonstrates the extent of breast development and hair growth is available for comparison. Thelarche or breast development is followed by axillary and public hair growth (adrenarche/pubarche). This is followed by menarche, which marks the onset of menstruation in girls. Menarche occurs in SMR stage 2 onwards usually 2 years after breast development and 1 year after pubarche. In 10% girls, menarche occurs during SMR 2, in 80% during SMR 3 to 4 and in 10% during SMR 5. Early adolescence is SMR 1 to 2, mid-adolescence is SMR 3 to 4 and late adolescence is SMR 5.

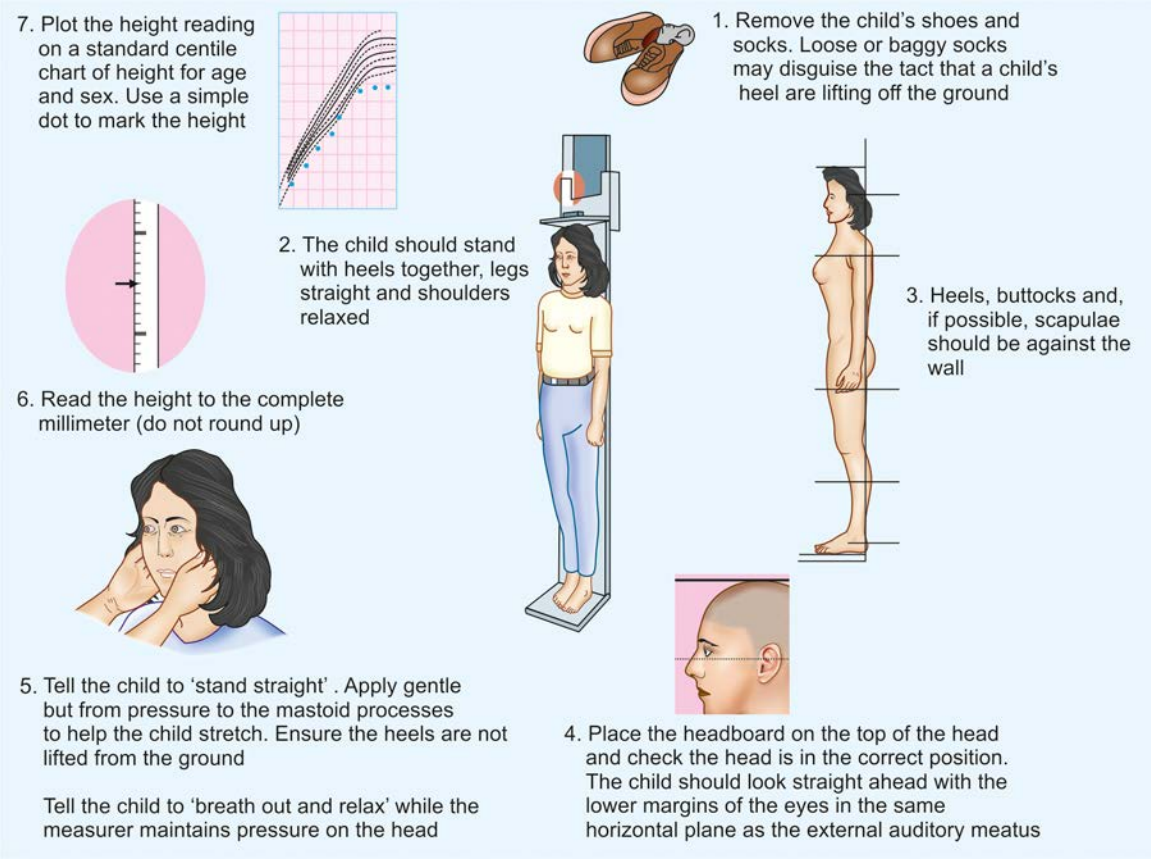


Fig. 35.4: Measurement of height

In boys, increase in testicular size is the first sign of puberty, followed by enlargement of genital organs, adrenarche, spermarche and facial hair growth. Voice change also occurs during puberty. During puberty, growth spurt occurs and up to 26 to 28 cm height gain can be expected. Prader's Orchidometer is used for assessing the size of the testes (Tables 35.15 and 35.16).

The onset of puberty is variable. Some kick off puberty early and their growth also stops early leading to shortness of stature. Those who enter puberty later, get a longer period to grow and tend to become taller.

Assessment of Development

Gross motor, fine motor adaptive, language, personal social development, developmental age, development quotient (DQ), School performance, intelligence, etc.

Development occurs in a cephalocaudal sequence and the milestones are attained at almost the same age among normal children. The milestones are categorized into 4 groups;

1. gross motor,
2. fine motor adaptive,
3. language and
4. personal social development.

The four important key milestones are the following:

1. Social smile	Not later than 2 months
2. Head control	4 months
3. Sitting without support	8 months
4. Upright and making a few steps with or without support	12 months

Also ensure that the vision, hearing and speech are normal (Table 35.17).

Developmental age is the average of the motor and mental performances as per the milestones.

Developmental quotient (DQ) is calculated as follows:

Tanner Sexual Maturity Scale

Table 35.15: Tanner sexual maturity scale for boys

Stage	*Genital development*	*Pubic hair*
1. Preadolescent	The testes, scrotum and penis are of about the same size and proportions as in early childhood	Preadolescent. No pubic hair
2.	Enlargement of the scrotum and testes. The skin of the scrotum reddens and changes in texture. Little or no enlargement of the penis	Sparse growth of slightly pigmented downy hair chiefly at the base of the penis
3.	Lengthening of the penis. Further growth of the testes and scrotum	Hair darker, coarser and more curled, spreading sparsely over the junction of the pubic bones
4.	Increase in breadth of the penis and development of the glans. The testes and scrotum are larger; the scrotum darkens	Hair adult in type, but covering a considerably smaller area than in the adult. No spread to the medial surface of the thighs
5.	Adult	Adult quantity and type with distribution of a horizontal pattern and spread to the medial surface of the thighs. Spread up linea alba occurs late, in about 80% of men, after adolescence is complete, and is rated Stage 6

Table 35.16: Tanner sexual maturity scale for girls

Stage	*Breast development*	*Pubic hair*
1. Preadolescent.	Preadolescent. Elevation of the papilla only.	Preadolescent. No pubic hair.
2.	Breast bud stage. Elevation of the breast and papilla as a small mound. Enlargement of the areola diameter	Sparse growth of slightly pigmented downy hair chiefly along the labia
3.	Further enlargement and elevation of the breast and areola, with no separation of their contours	Hair darker, coarser and more curled, spreading sparsely over the junction of the pubis
4.	Projection of the areola and papilla above the level of the breast	Hair adult in type, but covering a considerably smaller area than in the adult. No spread to the medial surface of the thighs
5.	Mature stage, projection of the papilla alone due to recession of the areola	Adult quantity and type with distribution of a horizontal pattern and spread to the medial surface of the thighs. In about 10 % of women, after adolescence is complete pubic hair spread sup the linea alba and is rated Stage 6

Table 35.17: Developmental milestones

Age	*Motor*	*Adaptive*	*Language*	*Social*	*Vision and hearing*
1 Month	Head lifts momentarily in the plane of body, ATNR (asymmetric tonic neck reflex) predominates, complete head lag, momentarily holds chin off the couch in prone position, sitting position-holds head up momentarily			Beginning to smile	Follows moving object, less than 90°, turns his head to rattle
2 Months	Head in plane of body, head lag partial, sitting position-head bobs, plane of face at 45° by raising chin recurrently	Hands predominantly closed	Coos	Social smile +	Follows objects 180°

Contd...

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Age	*Motor*	*Adaptive*	*Language*	*Social*	*Vision and hearing*
3 Months	Lifts head and chest, head above plane of body, moderate head control, bears weight on forearms	Reaches toward object and misses, hands open, no more grasp reflex, hand regard present, pulls at his dress	Says aah or naah, vocalizes with pleasure	Sustained social contact	Binocular vision develops by 3–6 months
4 Months	No head lag, head steady, enjoys sitting with full truncal support, when erect pushes with feet, ATNR gone, holds head and chest of couch	Reaches and grasps object and brings to mouth, approaches object and overshoots, Hands in midline and plays with them, pulls his dress over the face, plays with rattle when kept in hand		Laughs out loud, excited at sight of food and breast	Turns head towards a sound at the same level at 3–4 months
5 Months	Full head control,	Able to grasp objects deliberately, no more hand regard, crumples paper, plays with toys, bidexterous grasp	Smiles at self in the mirror	When he drops rattle looks to see where it has fallen	Turns head towards a sound below the level at 5–6 months
6 Months	Holds chest and abdomen on the couch, weight bearing on extended arms, rolls over from prone to supine	Grasps his feet and brings to mouth, holds bottle, if he has one cube in hand drops it if another is offered	Smiles and vocalizes at self in the mirror, monosyllabic babble	When he drops the rattle he tries to recover it, may protrude tongue as imitation, may show stranger anxiety, laughs when head is hidden in towel in peep -a- boo - game, beginning to show likes and dislikes of food.	
9 Months	Stands holding on to furniture, in trying to crawl may progress backwards, sitting-can lean forward	Brings 2 cubes together as if to compare the sizes and bangs them on the table		Puts arm in front of face to prevent mother from washing face.	
12 Months	Walks with one hand held, rises independently, bear walking	Unassisted pincer grasp, releases object to person on request, feeds with spoon with spilling	Few words besides mama or dada, 2–3 words with meaning	Plays simple ball game, may kiss on request, mimicry	
18 Months	Runs stiffly, sits on a small chair, walks upstairs with one hand held, walks normally, pulls toy as he walks, throws ball without falling	Makes tower of 4 cubes, imitates scribbling, imitates vertical stroke, dumps pellet in the bottle, feeds self-managing cup without spilling, turns 2–3 pages at a time	Average 10 words, names one or more parts of the body, points correctly to 1 picture, names 1 object	Feeds self, tells when wet or soiled, clean and dry with occasional accident, carries out 2 simple orders, uses stick to reach toy, dry by day	
24 Months	Runs well, walks up and down stairs, one step at a time, 2 feet per step, opens doors, jumps, climbs on furnitures	Tower of 7 cubes, circular scribbling, imitates horizontal stroke, turns pages one at a time, washes and dries hands	Puts 3 words together, talks incessantly, names 2 objects, tells a simple sentence	Handles spoon well, listens to stories with pictures, helps to undress, obeys 4 simple orders, dry at night, wears socks or shoes	

Contd...

Contd...

Age	Motor	Adaptive	Language	Social	Vision and hearing
30 Months	Goes upstairs with alternating feet, jumps with both feet, walks on tiptoe when asked	Tower of 9 cubes, makes vertical and horizontal stroke but generally not a cross, imitates circular stroke, forming closed figure, holds pencil in hand	Uses pronoun I, knows full name, names 3 objects, repeats 2 digits, sex organs	Helps put things away, pretends to play, beginning to take interest in	
36 Months	Rides tricycle, stand momentarily on single foot, goes upstairs with 1 foot per step and downstairs with 2 feet per step, jumps off bottom step	Tower of 10 cubes, copies a circle and imitates a cross (copies a cross by 3½ years), beginning to draw spontaneously or on request	Counts three objects, repeats 3 numbers or a sentence of 6 syllables, constantly asking questions, knows some nursery rhymes, vocabulary = 250 words	Knows age and sex, parallel play present, washes hands, helps in dressing and does by self if helped with the buttons, postpone toilet movement	
48 Months	Hops on one foot, throws ball overhand, climbs well, goes downstairs with one foot per step	Copies a square, draws a man with 2–4 parts, names longer of the 2 lines, uses scissors, tripod grasp	Counts 4 numbers correctly, tells a story, obeys 4 commands, tells tall stories	Plays with children, role playing present, goes to toilet alone, right – left discrimination, imaginative play with a doll, can button clothes fully	
60 Months	Skips	Names the heavier object, copies a triangle	Names 4 colors; counts to 10, distinguishes morning from afternoon, repeats 4 digits	Dresses and undresses; domestic role playing; asks questions regarding meaning of words	
66 Months		Copies a diamond	Repeats 5 digits	Knows number of fingers, names week days, names 4 coins	

$$DQ = \frac{\text{Developmental age}}{\text{Chronological age}} \times 100$$

A battery of tests is available for developmental assessment.

1. The denver developmental screening test (DDST). It was first designed by Frankenburg in 1967. It is suitable for a quick assessment in children, up to 6 years. It will take 10 to 25 minutes only. Development is assessed in four areas namely gross motor, fine motor adaptive, language and personal social.
2. Other assessment tools include Gessel Developmental Schedule (GDS), Bayley Scale of Infant Development (BSID), Baroda Developmental Screening Test (BDST).
3. **Trivandrum Developmental Screening Chart (TDSC).** It was designed by MKC Nair et al. in 1991 in the Trivandrum Child Development Centre (CDC). Seventeen items from the Baroda norms of BSID are selected. It is applicable up to 20 months of age. It takes only 5 to 7 minutes and can be administered with minimal training.
4. **Developmental Observation Card (DOC)** (Fig. 35.5). It was designed by MKC Nair et al. in 1992 in the Trivandrum Child Development Centre. Majority of developmental delays can be identified by observing the four key milestones namely social smile, head control, sitting and standing, which generally appear not later than 2,4,8 and 12 months, respectively. It is also important to ensure whether the baby has vision and hearing (Fig. 35.5).

INTELLIGENCE

It is the ability of knowing, understanding and reasoning.

Intelligence quotient (IQ) is computed as:

$$IQ = \frac{\text{Mental Age}}{\text{Chronological Age}} \times 100$$

Intelligence tests can be done in children above 3 years of age.

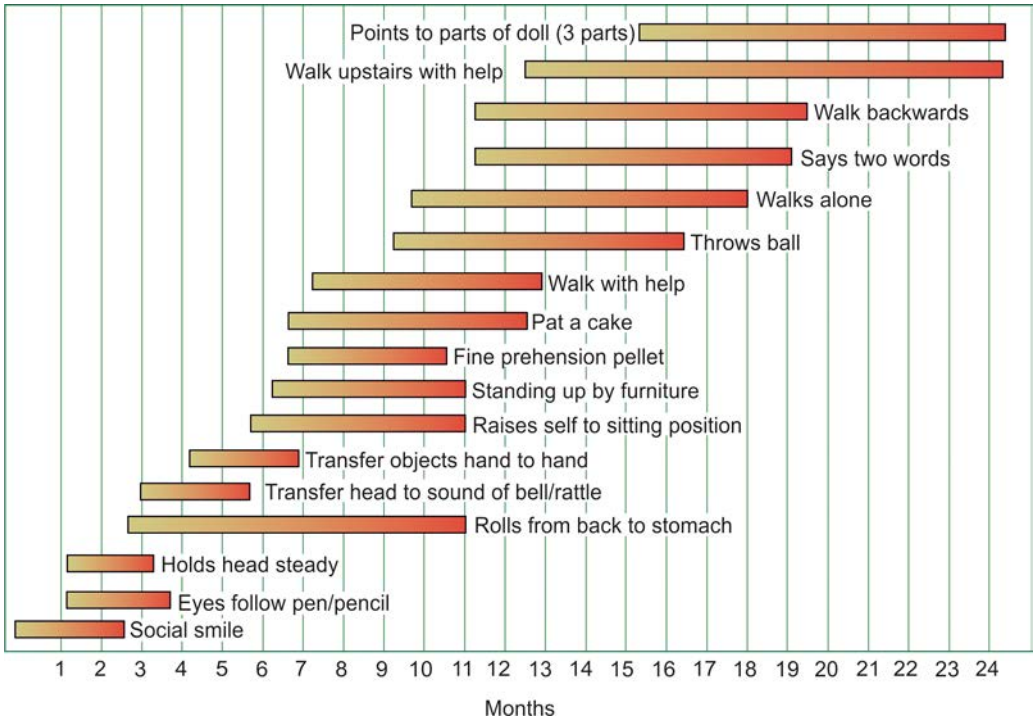


Fig. 35.5: Trivandrum Developmental Screening Chart (TDSC)
Ref – MKC Nair, Babu George, Elsie Philip; Indian Pediatrics 1991;28:869-72

Table 35.18: Systemic examination

System	*Differences between adults and children*
General examination	• Examination of infants is usually done in the mother's lap. Young children can be examined in the mother's lap or in the standing position. Older children co-operate to lie down for examination. • Normal range of vitals like pulse rate, BP, RR are age dependent (refer table) • Body proportion is different (refer Table). • Assessment of growth by anthropometry and development as per develop mental milestones should be undertaken. • Screen for congenital anomalies and dysmorphic/coarse facies features, e.g. down syndrome, mucopolyscharidosis, hypothyroidism. (refer Figures) Figs 35.6–35.9.
Cardiovascular system	• JVP is difficult to examine in infants. But is a useful tool in older children. • Location of apical impulse vary with age 4th left intercostals space just lateral to midclavicular line in infants to adult location by 5 year • Innocent murmurs unassociated with structural heart disease may be present in children. It is usually heard in pulmonary area due to the small size of pulmonary valve in children. • Still's murmur is an innocent short musical ejection systolic murmur heard at the lower sternal edge. • Features of congestive failure in infants include poor feeding, head sweating, suck-rest-suck cycle, tachycardia, tachypnea, tender hepatomegaly and cardiomegaly. • Sometimes S_3 and S_4 may be heard normally in children.
Respiratory system	• Large tonsils and adenoid hypertrophy is common in childhood • Type of breathing is abdomino-thoracic • In children, intensity of breath sounds are higher and have a bronchial-like quality (puerile breathing) • Short periods of apnoea up to 20 seconds may be normal in newborn. • Vocal fremitus is difficult to assess but vocal resonance may be assessed while crying in young children
Nervous system	• Developmental milestones may be used to assess the higher mental functions • Neurological examination in children should be informal • Cranial nerve examination: – Olfactory function assessment is difficult in young children – The normal visual acuity of 6/6 is reached only by 6 years

Contd...

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System	*Differences between adults and children*
	– Facial nerve may be evaluated while the child is smiling or crying – Startle response to sound can be used to assess auditory function in infants • Accurate assessment of sensory system examination is difficult in young children • Plantar response may be normally extensor in newborn period. So unilateral up-going plantar is more important than bilateral upgoing plantar till 2 years of age
Gastrointestinal system	• Abdomen is slightly protuberant • Liver may be normally palpable 1–2 cm below costal margin • Spleen tip may be normally palpable in infants

B. Systemic Examination (Refer respective Chapters 3–11 for details) Table 35.18

Systemic examination is in the same lines as is done for adults, but with modifications applicable for the child.

Summary

History and examination-salient points.

Diagnosis and Differential Diagnosis

Points in favor and against the diagnosis.

Investigations (Figs 35.6 to 35.10)

Apart from investigations relevant to the diagnosis of presenting symptoms, certain special tests are undertaken in children. In an infant with failure to thrive tests like TORCH screen-toxoplasmosis, HIV, syphilis, hepatitis B, rubella, cytomegalovirus and herpes simplex (IgG and IgM), karyotyping, thyroid function test, metabolic screen and others may be done. In children with short stature, height age, bone age and developmental age may be compared. In hypothyroidism, there is shortness of stature, delayed bone age and mental retardation, but in hypo-pituitarism, there is no mental retardation. Long bone X-rays are ordered in short stature, skeletal dysplasias and endocrine disorders.

General Principles in Treatment

- General/supportive care
- Specific management
- Writing of a prescription as per the weight/age of the child.

Prevention of Disease in Children—General Principles

Primary

General measures to improve nutrition and sanitation, prevent airborne, waterborne, vector borne diseases,



Fig. 35.6: Down Syndrome *Note:* The coarse facies, macroglossia



Fig. 35.7: Hypothyroidism

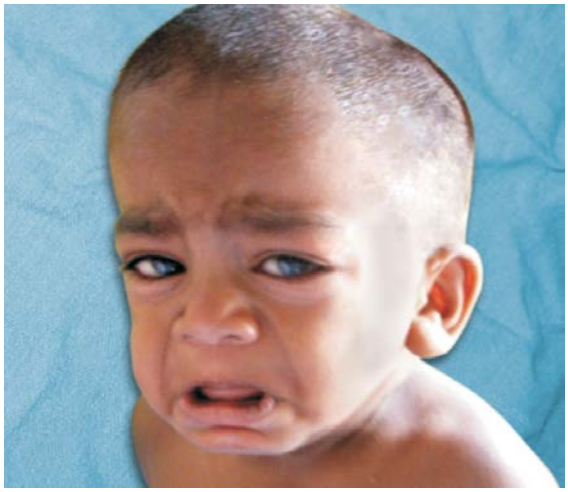


Fig. 35.8: Hurler's syndrome. *Note:* The coarse facies, abnormal shape of head and clouding of cornea



Fig. 35.10: Kwashiorkor. *Note:* The edema of the face, abdominen and limbs and skin changes over the face, legs and feet



Fig. 35.9: Marasmus. *Note:* The shriveled appearance, wrinkling of the skin and absence of subcutaneous fat

health promotion, early screening, pollution control, safe drinking water, public health engineering, biosafety and prevention of accidents.

Secondary

Specific protection, immunization, universal precaution for nosocomial and opportunistic infection and personal protection.

Tertiary

Disability limitation and rehabilitation.

NEWBORN BABY

Definitions

1. **Term Baby:** Babies born with from 37 weeks to less than 42 completed weeks of gestation (259–293 days)
2. **Preterm Baby:** Birth before 37 completed weeks of gestation (<259 days). The incidence is 8 to 10% of live births.
3. **Post-term Baby:** Birth after 42 or more completed weeks of gestation (>293 days)
4. **Low Birth weight** (LBW) Baby: Babies with a birth weight of <2500 g irrespective of gestational age. The incidence is 20 to 30% of live births. This forms 2 groups term LBW and preterm LBW.
5. **Very Low Birth Weight (VLBW)** Baby: Babies with a birth weight of <1500 g. The incidence is around 5% of live birth.
6. **Extremely Low Birth Weight (ELBW**) Baby: Babies with a birth weight of <1000g. The incidence is about 1% of live births.
7. **Appropriate for Gestational Age (AGA) Baby:** Babies with birth weight between 10th–90th percentile of the expected weight for the period of gestation as per intrauterine growth curves.
8. **Small for Gestation Age (SGA)** or Light for Date (LFD) / Small for Date (SFD) Baby: Babies with a birth weight <10th percentile for the period of gestation (as per intrauterine growth curves).

9. **Large for Gestation Age (LGA) Baby:** Babies with a birth weight >90th percentile for the period for gestation. In a term baby it is >4 kg.
10. **Neonatal Period:** Duration up to the first 28 days of life; Early neonatal period - Birth to < 7 days of life (168 hours) and late neonatal period – from 8 to 28 days of life.
 - **IUGR** refers to intrauterine growth retardation
 - **Low birth weight (LBW) Babies**
 - Those babies with weight < 2.5 Kg belong to mainly 2 types—preterm and term SGA babies.

Classification of SGA Babies

a. *Hypoplastic SGA Babies:* Babies with reduced growth potential due to abnormalities or insults during early part of gestation leading to internal or external congenital anomalies and reduction in weight, length and head circumference. These babies do not catchup with peer group, e.g. Down syndrome and intrauterine infections. These babies are called symmetric IUGR with Ponderal Index* of 2 to 2.5. (Normal is >2.5) Prognosis is guarded for such hypoplastic babies.

b. *Malnourished SGA Babies:* Babies with reduced weight due to placental dysfunction or maternal malnutrition during later months of gestation. Length and head circumference are normal and these babies often show adequate catchup growth. These babies are called 'asymmetric IUGR with Ponderal Index of <2. Their head circumferences will be at least 3 cm more than chest circumference. Prognosis is usually good.

c. *Mixed SGA babies:* Babies with adverse influences on growth and nutrition from the early part going onto later parts of gestation. They have features of both, hypoplastic and malnourished babies. Prognosis is guarded in them.

$$\text{* Ponderal Index} = \frac{\text{weight (g)}}{\text{length (cm)}^3} \times 100$$

Causes of SGA babies/intrauterine growth retardation (IUGR)

a. Maternal causes like: Malnutrition, PIH/ systemic diseases, addictions, medications and others.
b. Placental causes like: Placental dysfunction, multiple pregnancy.
c. Fetal causes like: Chromosomal anomalies, intrauterine infection, effect of teratogens.

Identification of preterm and term babies:

a. EDC calculation as per LMP
b. USS vise maturity assessment
c. Physical and neurological maturity.

Preterm babies look smaller and have extended posture, glistening skin and disproportionately large head. Physical and neurological maturity will help in differentiation. Various scoring systems are available like Dubowitz scoring system and New Bellard Score.

*The **Apgar score** is assessed at 1 minute and 5 minutes after birth to assess fetal neurological status and prognosis for survival and health (Refer chapter – 40).*

1 YCN – Infant and young child

Nutrition – This includes breastfeeding, complementary feeding, family pot feeding and supplementary feeding.

Breastfeeding

Breastfeeding should be initiated as soon as possible, preferably in half to one hour of delivery. Babies with 34 weeks gestational age and 1.8 kg weight at birth are generally stable. They can co-ordinate sucking and swallowing and can be put to breast and nursed in the same bed with mother. 'Rooming in' is the practice of keeping the mother and the baby in the same room. This will ensure better 'mother infant bonding (MIB) and better breastfeeding practices 'Bedding in' is the practice of keeping the mother and the baby together in the same bed. 'Mothering in' is the practice of placing the baby on the mother's chest and abdomen 'Kangaroo Mother Care' (KMC) is an innovative practice of keeping the baby with head turned to one side on the mother's chest in between the breasts, with naked body and only head cap and napkins. The baby is then wrapped up in shawl or in a special under cloth called 'Lycra'. The mother can wear a house coat over that without causing suffocation to the baby. She can take rest or move around with the baby close to the chest. This is, perhaps the cheapest and the best way to care for LBW or preterm babies. KMC can also be given by the father or any other care taker.

Observe all possible 'cleans' during delivery and newborn care in order to prevent sepsis (Table 35.19).

Table 35.19: Cleans during delivery

Five cleans
• Clean surface
• Clean hands
• Clean razor
• Clean cord tie
• Clean cord stump

Physiological jaundice occurs after 1 to 2 days and clears by 7 to 10 days. It is mild (5mg/dL), noticed only on the face. Jaundice occurring within 24 hrs of life and staining of palms soles is pathological. Physiological jaundice is due to reduced life span of RBCS (90 days vs 120 days in adults) and immaturity of the liver. Jaundice may be aggravated in prematurity, traumatic delivery, cephalhematoma, sepsis, constipation, dehydration and others.

Assess the time of onset and the severity of jaundice. Jaundice within 24 hours, persisting after 10 to 14 days and staining of palms and soles need investigation and referral.

Clinical Correlation of Jaundice with Skin Color (Kramer's) (Tables 35.20 and 35.21)

Table 35.20: Severity of jaundice

• Clinical jaundice	S. Bilirubin
• Face	5 mg/dL
• Up to nipple	7 mg/dL
• Face + trunk	10 mg/dL
• Face + trunk + thigh	12 mg/dL
• Face + trunk + legs	15 mg/dL
• Whole body + palms and soles	> 20 mg/dL

Table 35.21: Causes of Neonatal jaundice as per time of onset

<24 Hrs	*24–72 Hrs*	*>72 Hrs*
Blood group incompatibility (Rh, ABO and minor groups), Intrauterine infections, Maternal drugs such as Vitamin K, salicylates, sulfisoxazole, Hemolytic anemias, Criggler Najjar syndrome due to lack of conjugating glucuronyl transferase enzymes, Lucy Driscoll syndrome due to placental transfer of inhibitor of conjugation-ortho -amino phenol	Physiological jaundice, Exaggerated physiological jaundice, prematurity, acidosis, hypoxia, polycythemia, cephal hematoma, Hypothyroidism, All causes <24 hrs,	Neo sepsis, Neo hepatitis, Neo cholestasis, Biliary atresia, Breastmilk jaundice due to inhibitor of conjugation of 3-alpha 2-beta pregnanediol Intestinal obstruction, Pyloric stenosis, Metabolic causes- Galactosemia, tyrosinemia, hypothyroidism Inspissated bile syndrome, Intrauterine infections, Gilbert's syndrome due to mutation of transferase enzyme gene, Rotor and Dubin Johnson syndrome due to excretory defects

Neonatal Reflexes

Neonatal reflexes are given in Table 35.22.

Table 35.22: Neonatal reflexes—age of onset and disappearance

Reflex	*Age of onset*	*Age of disappearance*
Moro	Birth	12 weeks
Stepping	Birth	6 weeks
Placing	Birth	6 weeks
Sucking	Birth	4–7 months
Rooting	Birth	4–7 months
Palmar grasp	Birth	4–6 months
Plantar grasp	Birth	10 months
Tonic neck	2 months	4–6 months
Landau	3 months	24 months
Parachute	9 months	Persists

Gestational age— Assessment

The assessment of gestational age is done by examining physical and neurological criteria – Tables 35.23 to 35.25.

Table 35.23: Assessment of gestational age—physical criteria

Criteria	*Score 0*	*1*	*2*	*3*
Skin texture test by inspection and pinching	Very thin and gelatinous	Smooth, medium thickness with superficial peeling	Thick with peeling and cracking over hands and feet	
Lanugo hair-examine on the back	Nil/scanty	Abundant	Thinning at places	Scanty with bald areas
Plantar creases Assess after stretching the skin	NIL	Faint red marks over anterior half of sole	Deep indentations over anterior ½ of sole	Deep indentations throughout the sole
Breast nodule test by holding the breast tissue between thumb and finger	NIL	Breast tissue < 5mm on one or both sides	Breast tissue 5–10 mm	Breast tissue more than 10 mm diameter
Ear firmness assess by palpation	Pinna feels soft and easily folded into bizarre shapes. No recoil	Soft but some recoil present	Some cartilage felt along the edge and recoil present	Pinna firm with definite cartilage throughout and instant recoil
Genitalia • male	Neither testes in scrotum	At least one testis in the inguinal canal and can be pulled down into the scrotum	At least one testis present in the scrotum	
• Female	Labia majora widely separated and labia minora protruding	Labia majora partly cover labia minora	Labia majora completely cover the labia minora	

Table 35.24: Scoring system for assessment of gestational age-neurological criteria

Criteria	*0*	*1*	*2*	*3*
Posture: observe with infant quiet and in supine position	Arms and legs extended	Beginning of flexion of hips and knees. arms extended	Stronger flexion of legs and some flexion of arms	Legs flexed and abducted while arms completely flexed.
Arm recoil in a supine infant, the flexed forearm is extended by pulling at hands and then released	No recoil or only random movements	Arms return to incomplete flexion or sluggish response	Arms briskly returns to full flexion	
Popliteal angle	180 degree	180–150	150–120	120–90
Head lag	Complete head lag	Partial head control	Able to maintain head in line with the body	Brings head anterior to the body
Glabellar tap- tap sharply at glabella (midpoint between eye brows) and look for closure of the eyes	Absent	Weak response	Brisk response	

Table 35.25: Combined total score and gestational age

Combined total score	*Gestational age weeks*
9	28
10	29
11	30
12	31
13	32
15	33
16	34
18	35
19	36
20	37
23	38
25	39
> 26	40

SECTION

13

Geriatrics

CHAPTER

36 Examination of Geriatric Patients

Aswini Kumar

General causes of morbidity in the elderly, Interrogation, Physical examination, Elderly women

INTRODUCTION

Geriatrics is that branch of medicine which renders care for the elderly.

Gerontology is the study of physical and psychological changes which are incidental to old age.

Elderly population forms three distinct groups-young-old (65-74 years), middle-old (75-84 years) and old (85 + years). The advances in medicine and improvement in health care delivery systems have led to more and more persons reaching the geriatric age group. The geriatric population is currently about 10% of the world population and it is expected to rise considerably in the coming century, when compared to the present century.

Present evidence suggests that people are now not only living longer than they did previously, but also they are living with lesser disability and fewer functional limitations. Most people may deteriorate physically before death but this process can be postponed, enabling people to live without dependency. Many can now seek employment, which do not require strength, but only knowledge and experience.

A large proportion of people in the age group of 60's and 70's also work part time and contribute to the economy. This advancement is probably due to early diagnosis, improved treatment, improvements in living conditions and the facilities for managing the disabled. However, it has been observed that women have more functional limitations than men of the same age group.

If the present trend of increase of life expectancy continues into the twenty-first century, many babies born now in developed countries are likely to celebrate their 100th birthday.

Aging is growing old, whereas *senility* is the deterioration of the vitality or lowering of biological efficiency. Primary ageing is genetically determined and hence it is irreversible. Secondary ageing is attributable to personal, social and environmental factors and hence this is modifiable.

Diseases in the geriatric age group differ from those in other age groups. They are characterized by:

a. Involvement of multiple pathologic processes in multiple organ systems
b. Atypical or cryptic presentation
c. Presentation at an earlier stage of disease
d. Rapid deterioration if unattended to
e. Greater frequency of complications
f. Breakdown of personal, family, social, economic and environmental situations.

GENERAL CAUSES OF MORBIDITY IN THE ELDERLY

a. Aging process, e.g. impaired vision, impaired hearing, osteoporosis
b. Disease processes, e.g. ischemic heart disease, spondylosis, osteoarthritis
c. Combination or interaction of both a and b
d. Loss of mobility and physical disability due to various forms of arthritis

e. A general increase in multiple symptoms have been observed
f. General fatigue, dizziness and tendency to fall, leg ulcers, musculoskeletal pain, hypertension and worsening of lung function.
g. Immune processes are diminished in the elderly and hence they are more susceptible to infections, particularly of the respiratory and urinary tracts.
h. The incidence of cancer also increases considerably as age advances. Prostate cancer in men, breast cancer in women and cancer of the colon and melanoma in both sexes show increased occurrence.

All these factors should be kept in mind while approaching an elderly patient.

INTERROGATION

History is often narrated by the patient himself or a relative or a social worker. It should be kept in mind that the presentation of diseases may be atypical. For example, acute myocardial infarction may often be silent and detected only by investigations, or the presentation may be atypical in that, the symptom may be breathlessness or confusion rather than chest pain. Infections may not often present with fever but on the other hand, the presenting symptoms may be disordered behavior, refusal of food or alteration in the mental state. Due to the impairment in memory and defective hearing, the physician may have to be patient while eliciting the history. Often repeated interviews may be required.

The past history should include details about medical illnesses like cerebrovascular disease, coronary artery disease, obstructive airway disease, acid peptic disease, infections, constipation, urinary obstruction, minor or major surgical interventions, anesthesia and accidents.

Personal history should include details about the occupation, diet, physical activity, addictions, bowel habits and social behavior. In elderly female, patients' history of postmenopausal bleeding should be particularly asked for.

Drug history should be elaborated and this should elicit details about both prescribed and self-administered drugs, the time of starting and stopping the drugs, dosages, side-effects, withdrawal syndromes and drug allergies. Immunization status against influenza, pneumococcal infections, hepatitis and tetanus should be ascertained. The elderly are often non-compliant with prescribed medications. In many cases, they resort to self-medication with several drugs derived from different systems of medicine.

Social factors like status in the family, income, change of residence, interaction with family members and neighbors should be recorded. Death of a near relative especially of the spouse among an elderly couple is serious, resulting in severe psychological trauma; and in many cases this may precipitate the death of the survivor.

PHYSICAL EXAMINATION

This is basically the same as in other age groups. However, physical examination may require more than one session because the patient may become fatigued and uncooperative.

Assessment of nutritional status is important, since the elderly are more prone to suffer from malnutrition.

In general hemoglobin levels are lower in the elderly group. The reasons for this are not completely understood. In an individual patient, it may be that some decline in hemoglobin level occurs as part of aging but anemia is not only a consequence of aging. Malnutrition, loss of teeth, financial dependence, co-morbidities like chronic kidney disease, cardiac failure, COPD and drugs like NSAIDs, anti-coagulants and others may be contributing to anemia. Senescence which is a decreased capacity of the bone marrow to proliferate and regenerate in response to development of anemia may also contribute.

Several age-related changes and pathological phenomena are common in the elderly. These include the following:

Skin, hair and nails: The skin is often lax and shows wrinkles, furrows, xerosis and evidence of pruritis. *Petechiae* and purpura over the extremities subjected to minor trauma are common findings.

Campbell de Morgan's spots are commonly seen over the trunk and abdomen. These are non-pathological. In bed-ridden or chair-bound patients, pressure sores may be seen at pressure points such as the sacrum, hips, heels and other regions.

Grading of bed sores:

i. Soft tissue swelling
ii. Skin ulcer
iii. Skin and subcutaneous tissue ulceration
iv. Skin, subcutaneous tissues and deep fascia ulceration exposing underlying bone.

Malignancies: With advancement of age, the incidence and prevalence of cancers also increase.

Common sites for malignancy include the genital tract (especially the prostate), colon, stomach, skin, lungs, intracranial structures, lymphatic tissues and others. Any bizarre symptom occurring in the elderly should raise the suspicion of malignancy.

Nervous System and Special Senses

Physical examination should be directed to detect special problems such as sensory deficits, musculoskeletal dysfunction, urinary and fecal incontinence, gait problems and impairment of mental status. The mental state is rapidly assessed by using the modified minimental status examination. The senses of smell, taste, vision and hearing show age related impairment.

Muscles show wasting. Muscle tone may be increased. Superficial reflexes are less brisk.

Ankle jerk and knee jerk may be diminished or lost even in the absence of any other major neurological disease.

Primitive reflexes like *glabellar tap*, *sucking reflex*, *rooting reflex*, snout reflex and palmomental reflex may appear. This suggests the onset of diffuse irreversible brain damage.

Sensory abnormalities include impairment of pain sensation, paresthesia, anesthesia and diminution of vibration and proprioception.

Involuntary movements are common. These include titubation (rhythmic head nodding) and senile tremors of hands and legs. Parkisonism is more common. The gait is often short and shuffling. Neurological disability and painful osteoarthritis of the knees, hips and ankles adversely affect the stance and gait. They predispose to falls.

Eyes

Arcus senilis, enophthalmos and ptosis are common. Cataract is a common age-related problem which is often accelerated by pathological processes. Complete examination to assess the visual acuity, visual fields and ocular tension should be undertaken in all patients, since eye problems are common causes of disability. The pupils are often small and at times, may be irregular even without specific disease.

Ears

Inspissations of wax is the most frequent cause of reversible deafness. Presbyacusis is age related irreversible deafness. Full investigation is necessary to provide corrective hearing aids.

Cardiovascular System

The pulse rate decreases with increasing age. Sinus arrhythmia may not be present. Systematic palpation of all peripheral pulses and auscultation over both carotids should be done in order to detect occlusive vascular disease.

Blood pressure should be recorded in the lying, sitting and standing positions in order to detect postural hypotension. Fall in systolic blood pressure of more than 10 mm Hg may be seen during standing. Dysautonomia is the common cause for this. Systolic hypertension over 160 mm Hg is more common. Age related calcification of aortic and mitral valves may give rise to cardiac murmurs. Cardiac failure increases in frequency with age reaching up to 5 to 10% in people aged above 75 years.

Respiratory System

The usual respiratory rate at rest is 15 per minute. Expansion of the chest is diminished due to emphysema and changes in the thoracic cage. Tobacco-related diseases, COPD and respiratory infections are common. These increase the risk of morbidity and mortality due to acute infections such as influenza, pneumonia.

Gastrointestinal System

Loss of teeth is common and this leads to nutritional problems. Glossitis, cheliosis, angulo-stomatitis, ulceration of the angles of the mouth caused by dentures and poor oral hygiene are all common. Impairment of the senses of smell and taste lead to further diminution of food intake.

Abdominal palpation may reveal loaded sigmoid and rectum and distended urinary bladder. Rectal examination is mandatory to detect enlargement of the prostate, colonic lesions and the presence of *inspissated* fecal mass which may lead to spurious diarrhea and fecal incontinence.

ELDERLY WOMEN

Many women in India can be expected to live for twenty to thirty years after menopause. Due to hormonal changes and increase in risk of atherosclerosis, the incidence of coronary artery disease increases equal that in men after varying periods. Other common pathological conditions

include osteoporosis, osteopenic fractures and bone pains, which add to their disability and quality of life. Gynecological problems includes *pruritis vulvae*, senile atrophy of the vagina, uterus and adenexa, prolapse of the uterus and urinary and fecal incontinence. These cause great discomfort and also lead to social problems. Pelvic examination should be performed in women who have abdominal and pelvic problems. Even in asymptomatic patients pelvic examination is a must to detect occult malignancy.

The functional capacity of the patient should be assessed particularly to decide whether the patient can live an independent life without support. This can be done by using Barthel's index.

CONCLUSION

The elderly patients reveal several phenomena which include age-related changes and pathological findings. Several diseases are more common in them. The common causes of death in the geriatric age group are ischemic heart disease, respiratory infection, strokes and cancer.

Many physicians adopt a syndromic approach while treating geriatric patients. This takes into consideration the functional disabilities such as restriction of movement, diminution of vision, falls and so on, irrespective of the exact pathological causes. Maintenance of physical and psychological independence and reduction of the ill effects of age-related phenomena and diseases is one of the main goals of *geriatric medicine*.

Several indices have been designed to assess the pathological conditions in the elderly. *Hachinski score* distinguishes between dementia caused by ischemic brain lesions and nonischemic lesions. The *Barthel's index* is an assessment of functional capacity.

Hachinski Score for Ischemic versus Nonischemic Dementia

Feature	*Score*
• Abrupt onset	2
• Stepwise course	1
• Somatic features	1
• Emotional incontinence	1
• Systemic hypertension	1
• History of strokes	2
• Focal neurological symptoms	2
• Focal neurological signs	2

Interpretation

- Score > 4 indicates multi-infarct dementia
- Score < 4 indicates nonvascular dementia

Barthel's Index of Activities of Daily Living

Bowels	
• Continent	2
• Occasional incontinence	1
• Constant incontinence	0
Bladder	
• Continent	2
• Occasional incontinence	1
• Constant incontinence	0
Feeding	
• Independent	2
• Needs some help	1
• Dependent	0
Combing hair, washing face cleaning teeth and shaving	
• Independent	1
• Needs help	0
Dressing	
• Independent	2
• Can do half	1
• Dependent	0
Transfer (mobility)	
• Independent	3
• Minor help needed	2
• Major help needed	1
• Dependent	0
Using the toilet	
• Independent	2
• Needs some help	1
• Dependent	0
Walking	
• Independent	3
• Walks with one stick	2
• Wheel chair	1
• Dependent	0
Climbing stairs	
• Independent	2
• Needs some help	1
• Dependent	0
Bathing	
• Independent	2
• Needs some help	1
• Dependent	0

The total score is ascertained immediately after the onset of illness and repeated periodically on follow-up. Thereby improvement or deterioration can be assessed objectively.

SECTION

14

Pregnancy

CHAPTER

37 Maternal Changes in Pregnancy

V Rajasekharan Nair

General considerations, Hematological and cardiovascular changes, Pregnancy norms in Indian women

GENERAL CONSIDERATIONS

Pregnancy causes profound anatomical, physiological, and biochemical changes in the mother. Average weight gain during pregnancy is approximately 12.5 kg. This increase in weight during pregnancy is due to the uterus and its contents, the breasts, increases in blood volume and fluid retention and deposition of new fat and proteins (Fig. 37.1).

The uterus changes from its pear shape to globular shape by 12 weeks and becomes ovoid in the later weeks of pregnancy. It changes from a solid structure weighing about 70 g and with a capacity of 10 mL in the nonpregnant state to a thin-walled muscular sac weighing about 1100 g and with a capacity of 5 L or more to accommodate the fetus, placenta, and amniotic fluid during pregnancy. This is achieved mainly by marked hypertrophy and stretching of muscle cells whereas hyperplasia is limited. Uterine enlargement is most marked in the fundus, so that in the later months, the fallopian tubes and round ligaments are located slightly above the middle of the uterus (Fig. 37.2).

The stratification of the uterine musculature into an outer hood like layer of longitudinal fibers, a thick middle layer of interlacing network of muscle fibers and an internal sphincter-like layer becomes more marked during pregnancy. The blood vessels traverse the middle layer in such a way that when the muscles contract after delivery the vessels are constricted and the bleeding is arrested.

After 12 weeks the enlarging uterus becomes an abdominal organ and becomes more dextrorotated. In the supine position, the enlarged uterus falls back to compress the great vessels, especially the inferior vena cava and aorta. The irregular painless contractions in the first trimester becomes more marked in the second trimester. They are unpredictable, sporadic, and nonrhythmic and in the late third trimester becomes frequent, rhythmic and merge with the labor contractions at term.

The blood supply to the uterus increases from the nonpregnant level of 100 mL/minute to 1 to 1.5 L/minute at term. Uteroplacental blood flow increases progressively during pregnancy, ranging from approximately 450 to 650 mL/minute near term.

The cervix is markedly softened and bluish in the first month of pregnancy due to increased vascularity and edema. There is hypertrophy and hyperplasia of the cervical glands and eversion of the proliferating columnar endocervical glands which produce copious amounts of tenacious mucus that obstruct the cervical canal. It is rich in immunoglobulins and cytokines. At the onset of labor, this mucus plug is expelled. When dried on a glass slide, the cervical mucus shows the characteristic beading pattern as a result of progesterone.

Ovarian follicular maturation ceases during pregnancy and corpus luteum produces progesterone for the early development of fetus. Ovarian vessels

enlarge and contribute to the blood flow to the pregnant uterus. There is increased vascularity and hyperemia in the skin and muscles of the perineum and vulva and softening of the connective tissue.

Breasts

Breast tenderness is often the first symptom of pregnancy. There is enlargement of the breasts due to glandular hypertrophy. The axillary tail enlarges and may become painful. Bluish dilated veins appear over the breasts. The nipples enlarge and become deeply pigmented, and erectile. Hypertrophic sebaceous glands called glands of Montgomery are seen prominently in the areola. Thick, yellowish colostrum can be expressed from the nipples. Striae may appear on the skin (Fig. 37.1).

Skin

Cutaneous blood flow increases making the skin feel warm. Striae gravidarum or stretch marks develop in the abdominal skin and sometimes in the skin over the breasts and thighs. They appear as reddish, slightly depressed streaks. Later, they cicatrice and become glistening, silvery lines. Occasionally, diastasis of recti is seen which can lead to ventral hernia, if severe.

Hyperpigmentation is more common in those with darker complexion. The midline of the abdominal skin—linea alba—becomes especially pigmented, assuming a brownish-black color to form the linea nigra. Due to the progressive stretching of the abdominal skin, stretch marks called striae gravidarum tend to occur in all pregnant women. chloasma or melasma gravidarum—the so called mask of pregnancy are irregular brownish patches of varying size that appear on the face and neck. Pigmentation occurs in the areolae and genital skin also. After delivery hyperpigmentation regresses considerably. Angiomas or vascular spiders, telangiectasis and palmar erythema are due to vascular changes and are more common in white women (Fig. 37.3).

HEMATOLOGICAL AND CARDIOVASCULAR CHANGES

Maternal blood volume begins to increase during the first trimester and reaches 40 to 45% above the nonpregnant blood volume after 32 to 34 weeks. This hypervolemia helps to protect the mother and the fetus, against impaired venous return in the supine and erect positions and safeguards the mother against blood loss during parturition apart from meeting the demands of the hypertrophied vascular system and providing adequate nutrients to the rapidly growing placenta and fetus. Hypervolemia is mainly due to increased plasma volume than the erythrocyte volume

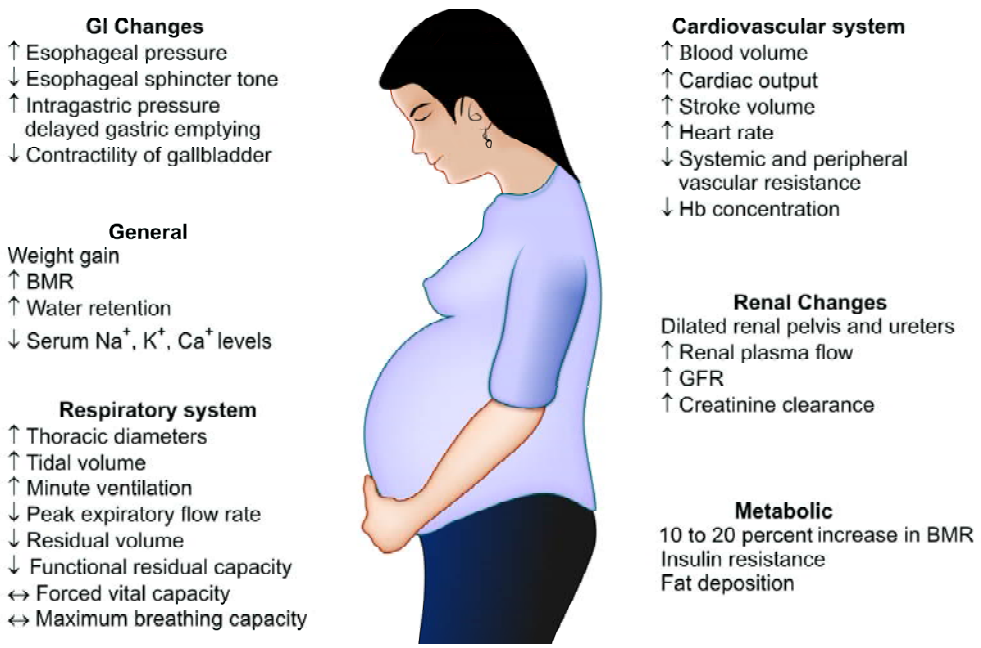


Fig. 37.1: Maternal changes in pregnancy

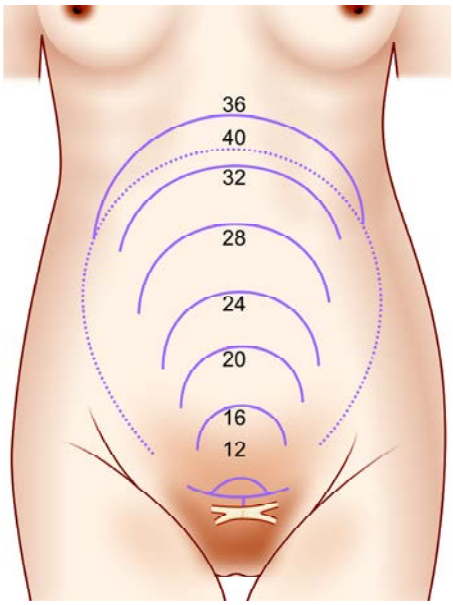


Fig. 37.2: Height of uterine fundus according to period of gestation in weeks

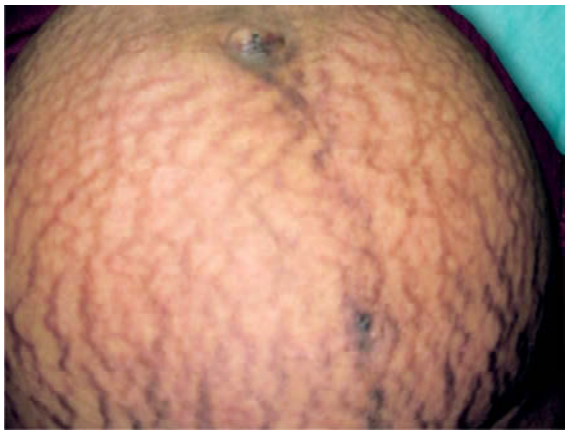


Fig. 37.3: Striae gravidarum and pigmentation of abdominal skin in pregnancy

and this leads to dilutional anemia. The increase in the erythrocyte volume averages about 50 mL. Moderate erythroid hyperplasia is present in the bone marrow and the reticulocyte count is elevated slightly during normal pregnancy due to the increase in maternal plasma erythropoietin levels. Hemoglobin concentration and hematocrit decrease slightly during pregnancy. Average hemoglobin concentration at term is 12.5 g/dL. Hemoglobin concentration below 11.0 g/dL is usually due to iron deficiency. Approximately 1000 mg of iron is required during normal pregnancy.

The iron requirement in the second half of pregnancy averages 6 to 7 mg/day. Iron is actively transferred to the fetus even when the mother has severe iron deficiency anemia. Serum iron and ferritin concentrations decline. During normal pregnancy, both coagulation and fibrinolysis are augmented. Concentrations of all clotting factors, except factors XI and XIII are increased and levels of high-molecular-weight fibrinogen complexes are also increased. Fibrinogen concentration increases approximately 50% to 300 to 600 mg/dL. The average platelet count is decreased slightly during pregnancy.

Cardiac output is increased as early as the fifth week due to reduced systemic vascular resistance and increased heart rate. The resting pulse rate increases about 10 beats/minute during pregnancy. Diaphragm becomes progressively elevated and the heart is displaced to the left and upward and rotated on its long axis leading to slight left-axis deviation in ECG. There is an exaggerated splitting of the first heart sound with increased loudness of both components; no changes in the aortic and pulmonary elements of the second sound and a loud, easily heard third sound. A systolic murmur may be present in 90% of pregnant women and a soft diastolic murmur in 20%. Continuous murmurs arising from the breast vasculature can be heard in 10%. During normal pregnancy, mean arterial pressure and vascular resistance decrease, while blood volume and basal metabolic rate increase. As a result, cardiac output at rest, when measured in the lateral recumbent position, increases significantly beginning in early pregnancy and remains elevated during the remainder of pregnancy. There is increase in heart rate, stroke volume, and cardiac output. Systemic vascular and pulmonary vascular resistance both decrease significantly, as also the colloid osmotic pressure. Pulmonary capillary wedge pressure and central venous pressure do not change appreciably Arterial pressure usually decreases to a nadir at 24 to 26 weeks and rises thereafter. Diastolic pressure decreases more than systolic. Venous blood flow in the legs is retarded during pregnancy. Supine

compression of the great vessels by the uterus causes significant arterial hypotension.

Respiratory System

The diaphragm rises about 4 cm and the subcostal angle widens so that as the transverse diameter of the thoracic cage increases approximately 2 cm and the thoracic circumference increases about 6 cm. Diaphragmatic excursion is actually greater in pregnant than in nonpregnant women. The functional residual capacity and the residual volume are decreased as a consequence of the elevation of the diaphragm.

Tidal volume and resting minute ventilation increase. Peak expiratory flow rates decline progressively as gestation advances. Lung compliance is unaffected by pregnancy, but airway conductance is increased and total pulmonary resistance reduced. The maximum breathing capacity and forced or timed vital capacity are not altered appreciably.

Urinary System

Kidney size increases slightly. There is dilatation of the renal pelvis and the ureters. Renal plasma flow increases early in pregnancy. The GFR increases as much as 25% by the second week after conception and reaches 50% by the beginning of the second trimester. About 60% of women report urinary frequency during pregnancy. Serum creatinine levels decrease during normal pregnancy from a mean of 0.7 to 0.5 mg/dL. Creatinine clearance in pregnancy averages about 30% higher than the 100 to 115 mL/min in nonpregnant women. Glucosuria during pregnancy may not be abnormal. Proteinuria more than trace amounts is abnormal. There is elevation, marked deepening and widening of the trigone of the bladder and thickening of its posterior, interureteric, margin. There are no mucosal changes.

Gastrointestinal Tract

Pyrosis (heartburn) is common during pregnancy due to reflux of acidic secretions into the lower esophagus as the lower esophageal sphincter tone is decreased and intraesophageal pressures are lower and intragastric pressures higher in pregnant women. The gums may become hyperemic and softened during pregnancy and may bleed when mildly traumatized. Hemorrhoids are fairly common during pregnancy. They are caused largely by constipation and elevated pressure in veins below the level of the enlarged uterus.

Total alkaline phosphatase activity almost doubles but much of the increase is attributable to heat-stable placental alkaline phosphatase isozymes. Serum aspartate transaminase (AST) alanine transaminase (ALT), glutamyl transferase (GGT) and bilirubin levels are slightly lower compared with nonpregnant values. The concentration of serum albumin decreases even though total albumin is increased. During normal pregnancy, the contractility of the gallbladder is reduced, leading to an increased residual volume. Impaired emptying leads to stasis, which is associated with increased bile cholesterol saturation of pregnancy. There is a propensity for intrahepatic cholestasis and pruritus gravidarum from retained bile salts in pregnancy.

Metabolic Changes

A smaller fraction of the increased weight is due to an increase in cellular water and deposition of new fat and protein—so-called maternal reserves. ***Average weight gain during pregnancy is approximately 12.5 kg***. Increased water retention is a normal physiological alteration of pregnancy leading to a fall in plasma osmolality.

Maternal basal metabolic rate is increased by 10 to 20% compared with that of the nonpregnant state. Additional total pregnancy energy demands are estimated to be as high as about 300 Kcal/day. Increase in water retention is mediated by a fall in plasma osmolality of approximately 10 mOsm/kg induced by a resetting of osmotic thresholds for thirst and vasopressin secretion. The minimum amount of extra water that the average woman accrues during normal pregnancy is approximately 6.5 L. This accumulation of fluid leads to pitting edema of the ankles and legs seen in most pregnant women.

At term the fetoplacental unit contains 500 g protein. The hyperplasia and hypertrophy of the uterine muscle along with the breast account for another 500 g. Amino acids in fetal circulation are at higher concentration than in maternal circulation.

Normal pregnancy is characterized by mild fasting hypoglycemia, postprandial hyperglycemia, and hyperinsulinemia. The purpose of this pregnancy-induced state of peripheral insulin resistance is to ensure a sustained postprandial supply of glucose to the fetus.

The concentrations of lipids, lipoproteins and apolipoproteins in plasma increase during pregnancy. There is fat deposition predominantly in central sites. Very low density lipoprotein (VLDL), low density lipoproteins (LDLs), and high density lipoproteins (HDLs) are increased. These changes are mediated by estradiol and progesterone as well as increase in leptin and ghrelin levels.

During normal pregnancy, there is retention of about 1000 mmol of sodium and 300 mmol of potassium as a result of enhanced tubular resorption, but their serum concentrations are decreased slightly because of expanded plasma volume. Total serum calcium levels decline during pregnancy.The increased fetal demand for calcium is met by doubling of maternal intestinal calcium absorption mediated by 1,25-dihydroxyvitamin D_3. Serum magnesium levels also decline during pregnancy. Serum phosphate levels remain unchanged.

Endocrine System

The pituitary gland enlarges even though it is not essential for maintenance of pregnancy. Serum growth hormone levels increase predominantly due to placental growth hormone (GH) secretion. Serum prolactin increases markedly during normal pregnancy. There is moderate enlargement of thyroid gland and production of thyroid hormones is increased, but there is only a slight increase in the free hormone levels because of the increase of thyroid binding globulin levels as well. Parathyroid hormone plasma concentrations decrease during the first trimester and then increase progressively throughout the remainder of pregnancy. Calcitonin levels are higher than those in nonpregnant women. The serum concentration of circulating cortisol is increased, even though secretion is not increased, because of reduced metabolic clearance rate of cortisol. During early pregnancy, the levels of circulating corticotropin (ACTH) are reduced strikingly. As pregnancy progresses, the levels of ACTH and free cortisol rise. Aldosterone and deoxycorticosterone increase while serum and urine levels of dehydroepiandrosterone sulfate are decreased during normal pregnancy. Androstenedione and testosterone levels are increased during pregnancy.

CHAPTER

38 Antenatal Examination

V Rajasekharan Nair

History, General examination, Obstetric examination, Terms used to describe palpation findings, Pelvic examination, Assessment of Cephalopelvic disproportion, Antenatal advice

OBJECTIVE

- To diagnose pre-existing maternal diseases (e.g. heart disease)
- To screen/diagnose for any new onset diseases (gestational diabetes mellitus (GDM), pre-eclampsia)
- To identify whether there are any obstetric risk factors for mother
- To identify the normal growth and well being of fetus
- To know the presentation, position of fetus
- To rule out cephalopelvic disproportion
- To prepare the woman and her family for delivery

INTRODUCTION

Watch Word: Every Pregnancy is Special

Even though pregnancy is a physiological phenomenon, every pregnancy should be considered as a special situation and good quality care should be given to prevent complications. This is especially significant in modern times when couple opt for only one or two children.

HISTORY

- Age: Very young (<18) and elderly (>35) gravidas are at high risk of obstetric complications
- Duration of marriage: History of infertility has to be enquired into
- Gravida: Number of times she has become pregnant including the present one
- Para: Number of previous deliveries after viability, i.e. 28 weeks of pregnancy
- LMP: Last menstrual period
- Expected date of confinement (EDC): This is calculated using Nagele's formula by adding 9 months and 7 days to LMP. This is an arbitrary date. Very few women deliver on this date.

History of Present Pregnancy

First Trimester

Date of first positive pregnancy test any symptoms of pregnancy that requires attention like excessive vomiting, any bleeding PV, history of febrile illness, drug intake and other significant events should be obtained.

Second Trimester

Date of quickening, immunization, infections, history of bleeding, pain or leaking should be asked for.

Third Trimester

History regarding fetal movements, pain, leaking or bleeding, previous obstetric history details of each pregnancy including the year of pregnancy, any antenatal complications, mode of delivery/termination, any intrapartum complications, baby's birth weight, gender, Apgar score, any abnormalities, any postpartum problems, any use of contraception between pregnancies, etc. should be recorded.

Menstrual History

Ask about menarche, regularity of cycles, duration of bleeding and whether bleeding is excessive or scanty. If the cycles are regular, then the calculation of expected date from the last menstrual period by adding nine months and seven days gives the expected date of confinement (EDC).

Past Medical History

History of any past illness especially with reference to heart disease, renal disease, hypertension, diabetes, endocrine disorders, drug allergy, drug therapy and blood transfusion.

Past Surgical History

Ascertain details of general and gynecological surgery, type of anesthesia, problems during surgery and postoperative period.

Family History

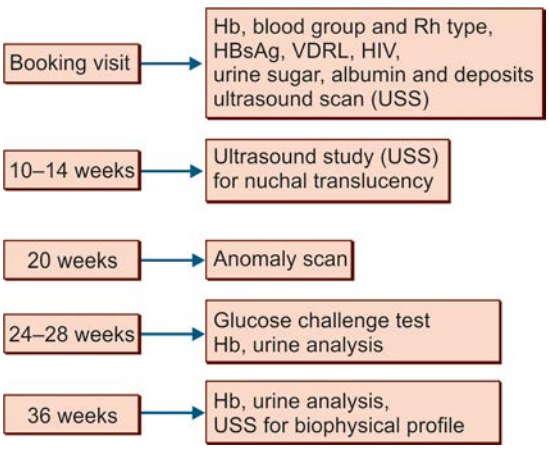
Record the incidence of diabetes mellitus, hypertension, other hereditary diseases, twinning and congenital anomalies in the family members.

Personal History

Find out details of addictions, contraception, allergies.

What to Do during each Visit (Flow chart 38.1)?

Flow chart 38.1: Antenatal care



GENERAL EXAMINATION

Build-large, medium or small, nutrition—adequate or poor.

Record Height and Weight

Pulse rate and character, pallor, jaundice, tongue, teeth, mouth, neck, throat, lymph node enlargement, edema, varicosities of veins in the legs.

Edema confined to ankles and disappearing after twelve hours of bed rest is a common finding in many and it is called physiological edema.

Breasts-pregnancy changes, state of nipples, lumps in the breasts.

Body Mass Index—Importance

Body mass index (BMI) wt in Kg/(height in m^2) is considered to be a very sensitive index of health and assumes greater significance in view of the increasing life style diseases. This can be arrived at from standard charts also. The prepregnant BMI is considered for assessing the individual's risk. BMI over 28 is associated with greater complications during pregnancy and puerperium. Apart from increase in medical complications like GDM, and pre-eclampsia these women run a higher risk of developing intrapartum, perioperative and anes thetic complications also. Many of these women require thromboprophylaxis, especially when they undergo operative procedures.

All systems should be examined routinely to detect abnormalities, if any, and to assess the changes induced by pregnancy.

Blood Pressure

Blood pressure should be recorded with the woman in sitting posture with the arm at the level of heart. BP is about 15 mm lower in lying down posture. In normal pregnant women systolic remains between 100 to 120 mm and diastolic between 70 and 80 mm mercury. If the recorded blood pressure is 140/90 mm or more on any occasion, it should be taken as abnormal. In those on antenatal follow-up, a rise of 20 mm in systolic or 15 mm in diastolic over the first trimester blood pressure is considered as hypertension.

OBSTETRIC EXAMINATION

Vaginal Examination During First Trimester

Vaginal examination is indicated if the patient presents before 12 weeks of gestation. It is done to confirm pregnancy and to ascertain whether it corresponds to period of gestation, whether it is intrauterine or extrauterine and whether other pelvic pathology like fibroids or ovarian tumor is associated with it (Fig. 38.1).

If vaginal discharge is present, a specimen of the discharge is taken for bacteriological examination using a speculum. The cervix is next inspected for discoloration, erosion and growths and a Papanicolaou (Pap) smear may be taken for cytological screening.

Abdominal Examination

The patient should empty the bladder and is put on the table in the dorsal position with the knees and thighs slightly flexed. Whole abdomen is exposed. The clinician stands on the right side of the patient.

Inspection

The contour of the abdomen, position and eversion of umbilicus, skin condition including striae gravidarum, linea nigra, excoriations and scars over the abdomen and presence of dilated veins are noted. Abnormalities such as over distension, subumbilical flattening and others should be looked for.

Palpation-Fundal Height

With the right palm make the uterus a midline structure and with the ulnar border of the left hand feel for the top of the fundus. Note the height of fundus in relation to the umbilicus and symphysis (Fig. 38.2). At 12 weeks uterus is just palpable above the symphysis. The distance between umbilicus and symphysis is divided into 3 equal parts. The lower 1/3 is reached at 16 weeks, 2/3 is reached at 20 weeks and uterus is at the umbilicus at 24 weeks. After the twentieth week the uterus rises at the rate of 1 cm every week. The distance between the umbilicus and xiphisternum is divided into three equal portions. Lower 1/3 is reached at 28 weeks, lower 2/3 at 32 weeks and the xiphisternum at 36 weeks. Thereafter, the height of the fundus descends and at 40 weeks it occupies the height at 32 weeks. This descent is due to engagement of the fetal head and the falling forward of the uterus.

Symphysiofundal height and abdominal girth also help to assess the normal growth and to rule out conditions such as intrauterine growth restriction (IUGR) or multiple pregnancy.

Leopold Maneuvers

Fundal Grip

This maneuver helps to determine the pole of the fetus (cephalic or podalic) which occupies the uterine fundus. The examiner stands on the right and places both hands with the palms down and fingers touching each other over the fundus and the fundus is palpated between these two hands (Fig. 38.3). If it is a breech, it will appear soft and regular and cannot be independently moved from the body. If it is head, it is rounded, hard and can be moved independently. In transverse lie, no part of the fetus will be found at the fundus.

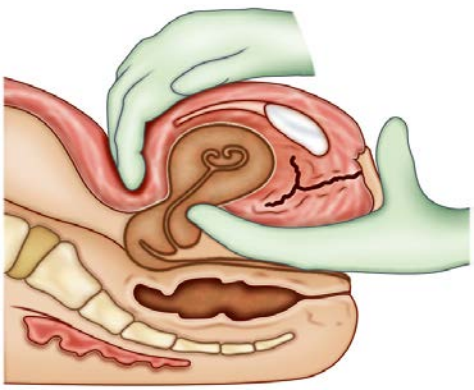


Fig. 38.1: Vaginal exam–early pregnancy showing elicitation of Hegar's sign (due to softening of cervix)



Fig. 38.2: Measuring height of fundus after correcting dextrorotation of uterus

Umbilical Grip

This helps to identify the side occupied by the back and limbs. The two hands are brought down and placed on either side of the uterus, at the level of umbilicus. Steady the uterine wall with one hand and palpate with the other to find out the side of the back which is firm and uniformly curved. The nodular limb buds will be on the opposite side. In transverse lie the head will be felt on one side and the breech on the opposite pole (Fig. 38.4).

First Pelvic Grip (Pawlik's grip)

This is done to identify the part of the fetus which occupies the lower pole of the uterus. Place the right palm on the lower pole of the uterus and grip the part between thumb and fingers. Try to move the part of the fetus occupying the lower pole. If it is head, it is hard, rounded and may be ballotable. If breech, it is soft, irregular and not ballotable. In transverse lie lower pole is empty (Fig. 38.5).

Second Pelvic Grip

This is done to assess the attitude of the head and to know whether the head is engaged. The examiner stands facing the feet of the woman. The fingers of both hands are placed on either side of the lower part of the uterus and brought down till the head is felt by one hand. That hand is kept steady and the other hand is lowered till the opposite pole of the head is felt. The portion of the head felt on the side of the back is occiput and the opposite is sinciput. The levels of occiput and sinciput and their relationship are noted. If occiput is at a lower level than sinciput, the head is flexed. If both are at same level, the head is deflexed. If sinciput is at a lower level than the occiput, the head is extended. If the head is engaged only sinciput will be felt since the occiput would have entered the pelvic brim. If both occiput and sinciput are felt head has not engaged, i.e. it is floating (Fig. 38.6).



Fig. 38.3: Fundal grip–palpating for fetal parts in the upper pole



Fig. 38.5: First pelvic grip



Fig. 38.4: Umbilical grip-palpating fetal back and limbs



Fig. 38.6: Second pelvic grip–noting relative levels of sinciput and occiput

Auscultation (Fig. 38.7)

Fetal heart is auscultated over the back with the fetal stethoscope (Pinard's). Maximum intensity of fetal heart sounds in cephalic presentation is below the umbilicus, in breech it is above the umbilicus and in transverse lie, at the level of the umbilicus. Auscultation can also be done using the bell of the stethoscope, lightly kept over the abdomen in the region of the fetal thorax.

TERMS USED TO DESCRIBE PALPATION FINDINGS

Lie

Relationship of longitudinal axis of fetus to longitudinal axis of uterus. It can be longitudinal, transverse or oblique.

Attitude is the relationship of fetal parts to one another. In cephalic presentation head may be flexed, extended or deflexed (Fig. 38.8).



Fig. 38.7: Listening to fetal heart using Pinard's fetoscope

Presentation

Part of fetus occupying the lower pole of uterus cephalic, podalic or shoulder (Fig. 38.8).

Position denotes the relationship of a reference point on the presenting part to the four quadrants of the pelvis. In vertex presentation it is the occiput, in face presentation, it is the chin or mentum and in breech presentation it is the sacrum. Accordingly in a vertex presentation, the position can be left or right occipitoanterior or occipitoposterior engagement. This is the condition in which the greatest transverse diameter of head, i.e. biparietal diameter (BPD) has passed down the pelvic brim.

Abnormal Presentations

The commonest fetal presentation is vertex but in 4 to 5% situations, other fetal body parts become the leading point. The commonest abnormal presentation is breech followed by others such as shoulder, face and brow (Fig. 38.9). The labor becomes difficult in these cases, In shoulder presentation (transvers lie) and brow presentation, normal delivery is almost impossible without intervention.

PELVIC EXAMINATION AND ASSESSMENT OF CEPHALOPELVIC DISPROPORTION

This is usually done in all primigravidas who have completed 38 weeks of pregnancy and multigravidas at the onset of labor. During per vaginal examination, effacement, consistency, position and dialatation of cervix are assessed. Then feel for the sacral promontory with the fingers introduced into the vagina. Normally, the sacral promontory is not palpable. If this is palpable, it denotes reduction

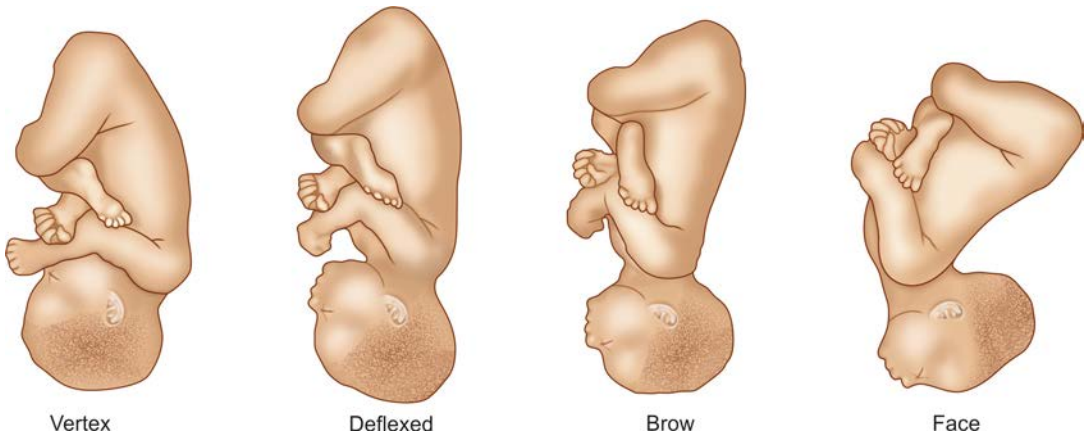


Fig. 38.8: Different cephalic presentations

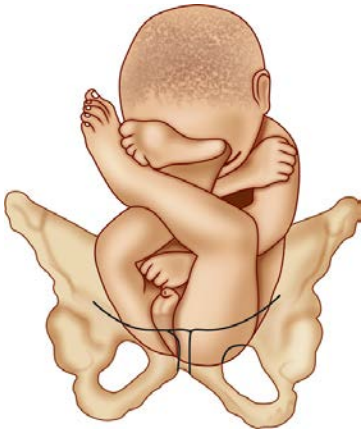


Fig. 38.9: Commonest abnormal presentation-breech

in anteroposterior diameter of the pelvic brim. Assess the distance from the sacral promontory to the undersurface of symphysis pubis, by making a mark on the palpating finger. This distance is the diagonal conjugate. The true anteroposterior diameter is 2 cm less than the diagonal conjugate. Feel for the hollow of the sacrum. Identify the sacrosciatic notches and ischial spines. Look for cephalopelvic disproportion by pushing the head down and feeling whether it comes down to the level of ischial spines. Feel for over-riding of the head by keeping the thumb over the symphysis pubic while the head is being pushed down. Subpubic angle is assessed by placing two fingers under the symphysis pubis. Normally, the subpubic angle should accommodate two fingers. Transverse diameter of the outlet is assessed by placing the knuckles in the widest part between the ischial tuberosities. Normally, four knuckles should be accommodated. The anteroposterior diameter is the distance from the tip of the sacrum to the undersurface of the symphysis pubic.

ANTENATAL ADVICE

During each antenatal visit the pregnant woman should be instructed to adhere to certain general norms.

Iron and Folic Acid Supplementation

Iron present in the food is insufficient to prevent anemia. Hence, the woman should take iron tablet (60 mg elemental iron) daily. This is usually started after 12th week as the woman may have nausea and vomiting during the first trimester. A pregnant woman need to take at least 100 iron tablets during pregnancy without which she is at risk of developing anemia. Folic acid supplementation in periconceptional phase is known to reduce congenital malformations. In later weeks it is useful in preventing and treating dimorphic type of anemia seen in about 20% of pregnant women.

Immunization

Immunization against tetanus is given to all women during pregnancy. Two doses at 6 weeks interval may be given.

Activities and Exercises

The pregnant woman is encouraged to continue the usual activities she is accustomed to. As the number of working women in the community increase, this is important. There is no proven effect for bed rest in pregnancy even in cases of threatened abortion. Women with cardiac disease, hypertension and other major systemic diseases are exceptions.

Dietary Advice

During pregnancy and lactation, the nutritional requirement increases. Extra allowance of calories and proteins are given with special emphasis on balanced diet. A model diet chart for pregnant woman is shown below:

Time	*Meal*	*Menu*	*Amount*
6.30 am	Early morning	Tea/Coffee	Sugar 10g Milk 150 mL
8.30 am	Breakfast	*Idli*/*Dosa*/*Appam* Or *Puttu*/*Upma* Fruit seasonal	3 nos 3 cups 1
11.00 am	Mid morning	Ragi/Rava	1 cup
1.30 pm	Lunch	Rice (cooked) Veg curry *Dal* curry Curd Salad	3 cup 1 cup 30 g of dry dal 60 mL 1 plate (300 g)
4.00 pm	Evening	Tea/Coffee Snacks	I cup 50 g
8.00 pm	Dinner	Rice/*Chappathi* *Dal* curry Veg curry Salad	3 cup/3 nos 1 cup 1 cup 1 cup (300 g)
9.00 pm		Milk	1 cup (200 mL)

N.B–Nonvegetarians can have one or two servings of fish/meat or egg, replacing the *dal* curry. If the woman is obese/diabetic or having renal disease, suitable alterations have to be made.

Fish 150-200 g
Meat 150-200 g
Egg 1-2 } per day

CHAPTER

39 Common Investigations in Pregnancy

V Rajasekharan Nair

Pregnancy tests, Antenatal investigations, Ultrasound investigations, Amniocentesis, Chorionic villus biopsy, Electronic fetal monitoring

PREGNANCY TESTS

Pregnancy tests are based on detection of human chorionic gonadotropin (hCG) in maternal blood and urine. Trophoblast cells produce hCG soon after implantation. This hormone is a glycoprotein with 2 subunits, named alpha and beta. The alpha subunit is identical to those of LH and TSH.

The hCG can be detected in maternal plasma or urine by 8 to 9 days after ovulation. The doubling time of plasma hCG concentration is 1.4 to 2.0 days. Serum hCG levels increase from the day of implantation and reach peak levels at 60 to 70 days. It is measured using immunoassays based on specific antibodies against the beta subunit.

The different techniques employed in urine pregnancy tests include sandwich type immunoassay, enzyme linked immunoassay, latex agglutination inhibition, direct latex agglutination and ELISA. While the former tests have a sensitivity ranging from 200 to 2000 IU/L, ELISA tests detect 20 IU/L. Urine tests usually become positive 2 days after a missed period.

Serum tests using radioimmunoassay can detect beta hCG 4 hours after fertilization. The sensitivity for the Laboratory detection of hCG in serum is as low as 1.0 mIU/mL. With extremely sensitive immunoradiometric assays, the detection limit is even lower.

False-positive hCG test results are rare. It is due to cross reaction with LH or heterophilic antibodies, which are human antibodies directed against animal-derived antigens, found in women who work closely with animals.

ANTENATAL INVESTIGATIONS

It is mandatory that all pregnant women should have Hb estimation, blood grouping and Rh typing and urine examination for albumin, sugar and deposits at the initial examination and repeated as per the clinical condition.

At present, in view of the increasing incidence of gestational diabetes, a routine glucose screen test, i.e. a standard 75 g oral glucose tolerance test (OGTT) as advised by WHO, is considered necessary in all pregnant women. Investigations like VDRL, HIV, and HBsAg are considered optional and may be done after discussion with the woman and her husband.

Urine culture and sensitivity tests are to be done if the deposits show pus cells.

Renal function, liver function and platelet counts are tested in patients with pre-eclampsia or kidney disease.

Rh negative mothers should have indirect Coombs' test (ICT) at booking, at 28 weeks and at 36 weeks, in order to detect Rh sensitization. If the Coombs' test is +ve in more than 1/16 dilution, serial amniocentesis and bilirubin level estimation will be needed.

A patient with thyroid swelling or known thyroid dysfunction would need thyroid function tests (TFTs)

or If she is on thyroxine or antithyroid drugs, TFT will have to be repeated in each trimester. Overt diabetics would need HbA_{1c} estimation and blood sugar estimations from the booking visit.

Testing for hemoglobinopathies, Down syndrome, neural tube defects and other abnormalities may be needed in specific situations as suggested by the history. Routine screening for trisomy 21, Trisomy 18 and neural tube defects by triple test at 15 to 20 weeks includes measurement of maternal serum alpha fetoprotein, hCG and estriol.

Screening for gestational diabetes: Routine screening for all pregnant women at 24 to 28 weeks is carried out with 75 gm OGTT (Oral GTT) as proposed by the World Health Organization. In those with higher risk of developing GDM earlier, the test is done during the booking visit itself. 75 OGTT is a single step challenge test where a fasting blood sugar is done followed by oral administration of 75 g glucose and estimation of the blood sugar at the end of 2 hr. This replaces the previous two stage investigation of doing a 50 g glucose challange first and the doing the OGTT if the blood sugar result goes beyond 140 mg/dL.



Fig. 39.1: Ultrasound measurement of biparietal diameter



Fig. 39.2: Measuring abdominal circumference a sensitive index in growth retardation

ULTRASOUND INVESTIGATION

Ultrasound scan is an extremely useful tool to follow the fetal development and detect abnormalities (Figs 39.1 and 39.2) (Flow chart 39.1).

Doppler velocimetry of the umbilical and uterine arteries is used to diagnose placental insufficiency. Middle cerebral artery Doppler is used for monitoring IUGR pregnancy.

AMNIOCENTESIS

Aspiration of amniotic fluid for genetic, bacteriological or biochemical studies is done between 14

Flow chart 39.1: Objectives of ultrasound examinations

First trimester	Confirm intrauterine pregnancy and exclude ectopic pregnancy, fetal viability, vesicular mole, missed abortion, multiple pregnancy, nuchal translucency and nasal bone for Down's syndrome screening, adnexal masses, fibroids and others
Second trimester	Detect fetal structural anomalies including cardiac anomalies Placental localization IUGR (Intrauterine growth retardation) Oligo/polyhydramnios
Third trimester	Fetal growth monitoring Placental localization Liquor volume Fetal weight Fetal well-being using biophysical profile

to 16 weeks under ultrasonographic guidance for genetic studies. At later gestations it may be required for monitoring of Rh sensitized pregnancy, decompressing a hydramnios or for confirmation of fetal lung maturity.

CHORIONIC VILLUS BIOPSY

It is done at 10 to 13 weeks transabdominally or transcervically helps to detect genetic abnormalities earlier. Percutaneous umbilical blood sampling (PUBS) or cordocentesis is another invasive technique for obtaining fetal blood sample for faster genetic analysis. Fetal tissue biopsy is possible to detect specific defects like muscular dystrophy or epidermolysis bullosa.

ELECTRONIC FETAL MONITORING

This can be used to assess fetal well-being in the antepartum period. Antepartum fetal surveillance is especially important for pregnancies complicated by IUGR, placental insufficiency, diabetes, PIH and others. Basal heart rate (120-180/min), beat to beat variability, presence of accelerations in heart rate during fetal movement (by15-20 beats and sustained for 15 to 20 seconds or more), any deceleration of fetal heart etc are noted. This is called a nonstress test (NST). A reactive NST is reassuring while a nonreactive NST may indicate fetal compromise.

Electronic fetal heart monitoring can be used for intrapartum monitoring of high risk pregnancies also (Fig. 39.3).

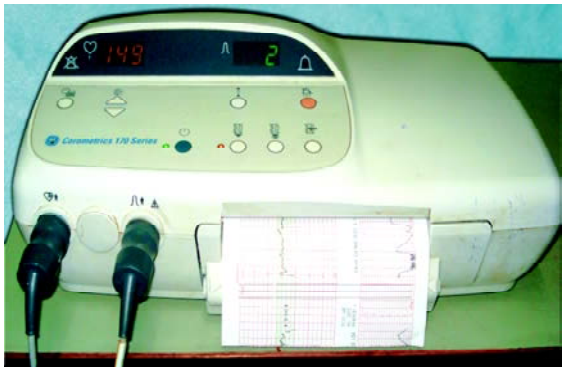


Fig. 39.3: Cardiotocograph used for monitoring fetal heart and uterine contractions

CHAPTER

40 Management of Normal Labor

V Rajasekharan Nair

Management of first stage, Management of second stage, Management of third stage, Fourth stage of labor, Instrumental deliveries, Cesarean section

Labor is the process by which childbirth occurs and represents the period from the onset of regular uterine contractions until expulsion of the placenta. It is marked by regular uterine contractions that bring about demonstrable effacement and dilatation of the cervix. The first stage of labor denotes progressive effacement and dilatation of cervix until it is fully dilated. The second stage starts at this point and ends with delivery of the fetus. The third stage of labor denotes the period from delivery of the fetus to expulsion of placenta and complete contraction and retraction of the uterus.

A patient may present at term with onset of labor pains, leaking or show (blood stained mucoid discharge). Duration of labor pains or leaking should be ascertained. Review the antenatal record and confirm the gravidity, parity, and period of gestation. Ascertain whether the gestational age is accurate by referring for early ultrasound. Look for any antenatal complications recorded in the antenatal chart. Vital signs including the pulse, blood pressure, temperature and respiratory rate are recorded. Obstetric examination is done at this stage. Abdominal palpation to ascertain the period of gestation, presentation and position of the fetus followed by assessment of frequency and intensity of uterine contractions and recording the fetal heart is done. Admission test is a cardiotocographic recording of the fetal heart tracing in relation to the uterine contractions and indicates fetal well-being. Enema is given unless there is bleeding PV or leaking with a mobile head. This is followed by a vaginal examination *unless there has been bleeding in excess of bloody show*. The procedure is done with all aseptic precautions. Examiner should wear mask and gloves after scrubbing the hands as for a surgical operation. The vulva is cleaned with antiseptic lotion and draped with sterile towels. Index and middle fingers of right hand lubricated with antiseptic lubricant are introduced into the vagina. The effacement and dilatation of cervix are noted. Obliteration of cervical canal is termed cervical effacement and is expressed as a percentage compared with that of an uneffaced cervix. When fully dilated, the cervix is 10 cm in diameter. Next step is to find out details of the presenting part and its position. In normal vertex presentation with occipito-anterior position, the posterior fontanelle will be felt in the anterior quadrant of pelvis. The posterior fontanelle is identified by the presence of three suture lines. The posterior fontanelle is in the posterior quadrant in occipito-posterior position. Station or the relationship of the head to the pelvis is noted. Level of the ischial spine is considered as O station. Look for caput formation or moulding which may indicate cephalopelvic disproportion.

MANAGEMENT OF THE FIRST STAGE

The normal laboring woman need not be confined to bed early in labor. She can assume any comfortable position. Prolonged supine position is to be avoided to prevent aortocaval compression.

Fetal well-being: The fetal heart rate should be checked immediately after a contraction at least



Fig. 40.1: Continuous monitoring of fetal heart and uterine contractions

every 30 minutes. Continuous electronic monitoring may be used with evaluation of the tracing every 15 minutes. Uterine contractions, intensity and duration of contractions are assessed electronically or manually (Fig. 40.1).

Maternal vital signs: Temperature, pulse, and blood pressure are evaluated at least every 4 hours. Food should be withheld during active labor and delivery. Clear liquids can be allowed. Establish an intravenous infusion line early in labor. Administration of glucose, sodium, and water to the laboring woman at the rate of 60 to 120 mL/hr prevents dehydration and acidosis.

Pain relief can be provided with opioid analgesics like pethidine, inhalation analgesia like nitrous oxide with oxygen or by administration of epidural analgesia.

If the urinary bladder gets distended the woman should be encouraged to void. Catheterization should be minimized. Periodic pelvic examinations are performed to evaluate labor progress and amniotomy may be performed once labor is well-established.

MANAGEMENT OF THE SECOND STAGE

When cervix is fully dialated, the woman starts bearing down and has an urge to defecate. Contractions increase in frequency and intensity. The maternal bearing down plays an important part in the expulsion of the fetus. When the head descends to the outlet, the perineum bulges and skin is stretched. Crowning of the fetal head indicates imminent delivery.

The woman is kept in the dorsal lithotomy position with the legs in stirrups. Vulva and perineum are cleaned and sterile drapes applied. The birth attendant should scrub, wear sterile mask, gown and gloves. A right mediolateral episiotomy is routinely applied in primigravidae and if perineal laceration is imminent in multigravidae. This is done after infiltration of the perineum with lignocaine. When the head crowns more than 5 cm at the introitus, it is delivered using modified Ritgen maneuver (forward pressure on the chin of the fetus through the perineum just in front of the coccyx and pressure exerted superiorly against the occiput by the other hand) or by gentle pressure with the left hand on the head while the flat of the right hand supports the perineum. This allows controlled delivery of the head.

Once the head is born it undergoes the movements of external rotation and restitution and assumes a transverse position. This indicates engagement of the shoulder. Gentle downward traction on the head may be necessary if the anterior shoulder is not born spontaneously. Drawing the head gently upwards helps delivery of the posterior shoulder. Rest of the body is born spontaneously.

As soon as the baby is delivered, the face is quickly wiped and the nares and mouth are aspirated to clear the airway and prevent aspiration of blood, mucus and amniotic fluid. Then the cord is clamped at two points and cut in between. Delaying the cord clamping until pulsations cease allow more blood to be transferred to the baby from the placenta. Then the clinical status of the baby is assessed and the Apgar score recorded taking into account the fetal heart rate, respiratory movements, color, cry, and attitude. Maximum score is 10.

Partogram

It is a composite record of all the events occurring during labor including the cervical dilatation, descent of head, intensity of uterine contractions, details of fetal heart sounds, liquor, drugs administered and maternal status. This is ideally suited to follow the course of labor and to initiate interventions such as augmentation including oxytocin acceleration, cesarean section and others. Partographic monitoring of labor is suitable for all settings, whether it is primary, secondary or tertiary (Fig. 40.2).

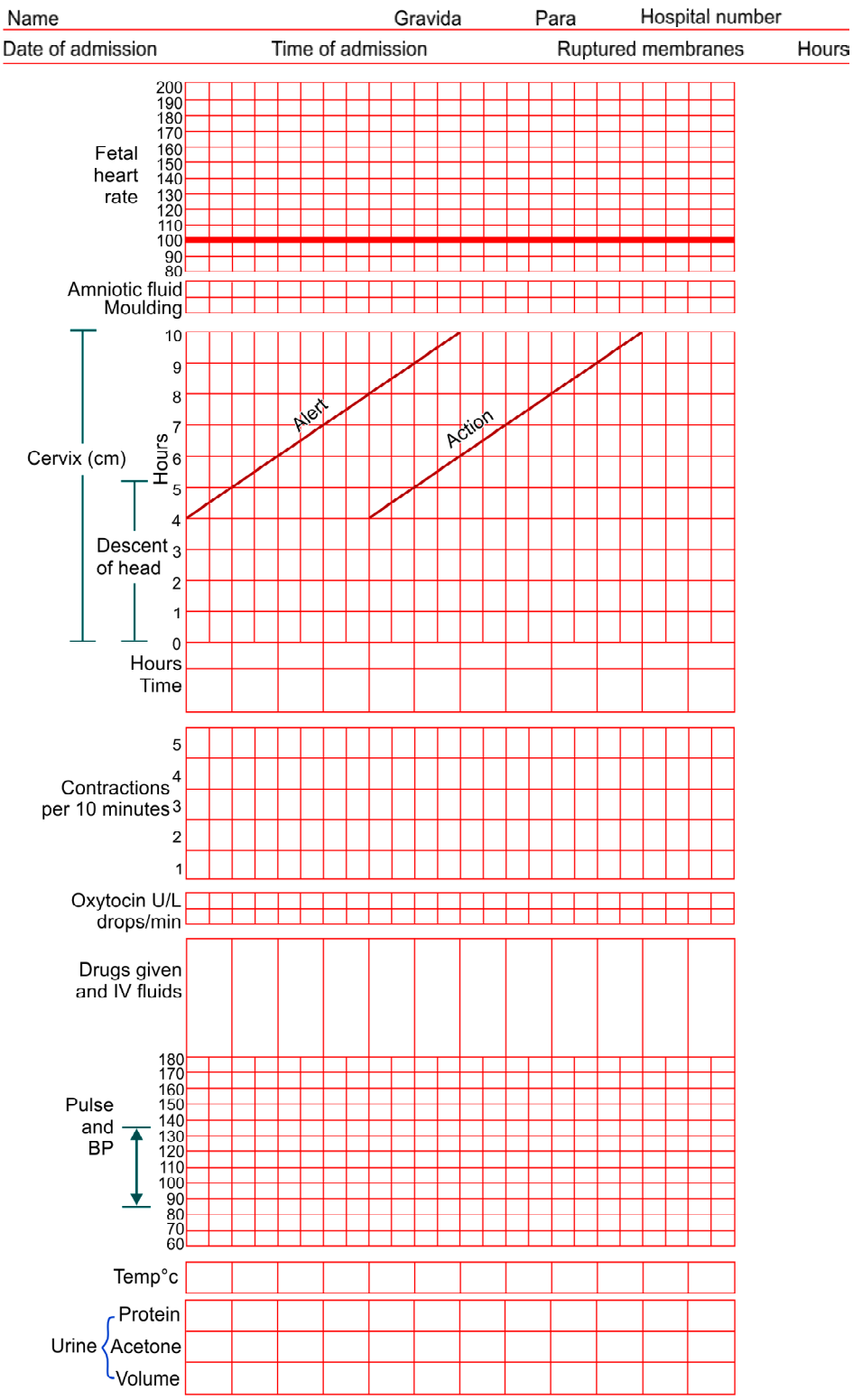


Fig. 40.2: WHO modified partogram

MANAGEMENT OF THE THIRD STAGE OF LABOR

After the baby is born, look for the signs of placental separation.

These include:

- The uterus starts becoming hard and globular
- Suprapubic bulging
- Extra vulval lengthening of the cord
- Fresh bleeding.

The expulsion of the separated placenta is aided by keeping the umbilical cord slightly taut and lifting the uterus cephalad with the abdominal hand. The uterus is massaged to make it contract and expel clots. Ten units of oxytocin is added to 500 mL normal saline and administered after delivery of the placenta at a rate of 10 mL/min (200 mU/min) for a few minutes until the uterus remains firmly contracted and bleeding is controlled. The infusion rate then is reduced to 1 to 2 mL/min until the mother is ready for transfer from the recovery suite to the postpartum unit. Then the infusion is usually discontinued.

Active Management of Third Stage of Labor

Third stage management is particularly important in the sense that, complications during this stage are sudden and constitute the most common cause for maternal mortality in India. Managing the third stage of labor in all parturients whether there is a risk factor or not by a definite protocol helps to reduce the occurrence of postpartum hemorrhage considerably. After the delivery of the fetus, 10 units of oxytocin (or 0.2 mg methergin) is given intramusculary to the mother, followed by delivering the placenta by controlled cord traction. Gentle massage of the uterus, and initiating the breastfeeding early will promote further uterine contraction and retraction and reduces the chance of postpartum hemorrhage. Routine adherence to active management of labor is a simple but useful intervention known to reduce maternal mortality significantly.

Examination of the Newborn and Apgar Score

First examination of the newborn is done in the labor room, to detect any gross congenital abnormalities and to establish a baseline for subsequent examinations. Apgar score is a scoring system intended to reveal neurological depression in the neonate. It is an indicator of brain damage sustained during or shortly after birth. In each of the five categories a score of 0,1 or 2 is given to give a maximum of 10 scores. The first examination is done at 1 minute after complete delivery disregarding the delivery of the cord and placenta. The second examination is done at 5 minutes. A score of 7 to 10 is good, 3 to 6 is moderate depression and 0 to 2 is severe neurological depression, when examined at 5 minutes. Apgar score at 5 minutes after birth is associated neurological deficit in about 10% of cases. Low Apgar score repeated at 5 minutes is a more accurate index to predict death and residual neurological disability.

Second detailed examination of the newborn is done probably in the postnatal ward, in the presence of the mother when she is completely resting. At this time minor variations of normal should be explained to the mother to avoid unnecessary maternal anxiety.

Schematic representation of stages of labor

Engagement	First stage of labor	Patient can move about withhold solid food, intravenous fluids, monitor fetal heart, contractions and maternal vital signs, periodic bladder emptying, pain relief, periodic pelvic examinations, amniotomy and oxytocin infusion as required
Descend with increasing flexion Internal rotation Extension Restitution External rotation	Second stage of labor	Dorsal/lateral position, aseptic precautions, lignocaine infiltration of perineum, right mediolateral episiotomy, controlled delivery of head, gentle traction to deliver shoulder, prophylactic methergine
	Third stage of labor	Wipe baby's face, clamp and cut the cord, clear the airway, placental separation and delivery
	Fourth stage of labor	2 to 3 hours following 3rd stage, administer oxytocics, repair of episiotomy, examine for local trauma and repair

Apgar score details–maximum total score–10

	Score allotted		
Clinical parameter	**0**	**1**	**2**
Heart rate	Absent	< 100	> 100
Respiration	Absent	Slow irregular	Regular
Muscle tone	Limp	Some flexion of extremities	Active movement
Response to catheter test (in nostril) after oropharynx is cleared	No response	Grimace	Cough or sneeze
Color	Blue pale	Body pink, extremities blue	Completely pink

FOURTH STAGE OF LABOR

The 2 to 3 hours immediately following the third stage of labor is critical, and it has been designated by some as the *fourth stage of labor*. Although oxytocics are administered, postpartum hemorrhage as the result of uterine atony is more likely at this time. Hence, the parturient should be closely monitored. Monitoring the general condition of woman by blood pressure and pulse rate, and palpating for the level of uterine fundus and the consistency of uterus and observing for any vaginal bleeding forms the basis of the vigilance. Slow trickle of blood occurring during this phase can cause deterioration of the maternal condition, which could be prevented by the above strategy.

INSTRUMENTAL DELIVERIES

In a small proportion of cases labor may not end spontaneously and this may necessitate interventions. If the fetal head has negotiated the pelvis very well and the vertex is well below the ischial spines, the delivery can be completed either with *vacuum extractor* or forceps depending on the situation. After delivery, the vagina and cervix should be inspected for any tears as this is more commonly seen following instrumental deliveries (Fig. 40.3).

CESAREAN SECTION

If conditions are not favorable for vaginal delivery, then delivery per abdomen–cesarean section should be thought of. This can be an elective procedure as in a case of placenta previa or abnormal presentation or can be an emergency procedure as in a case of



Fig. 40.3: Vacuum extractor (Ventouse)

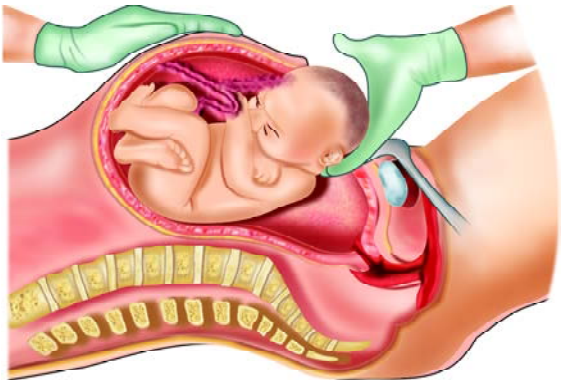


Fig. 40.4: Technique of delivering the baby during cesarean section

fetal distress due to various reasons. Regional anesthesia is preferred in most of the cases and the procedure is best done though a Pfannenstiel incision. In ideal situations, the incidence of cesarean section should be only around 15% of the total number of deliveries. Every attempt should be taken to reduce the number of primary cesarean sections (Fig. 40.4).

Who should Conduct a Delivery?

There is a false belief that all deliveries should be conducted by specialists. Delivery is a natural process, and in the majority of cases if there are no antenatal complications, it can be conducted by any trained person. Most problems occur during the second and third stage of labor which can be reduced by sticking on/to partograms and active management of third stage of labor. In India as a whole only 50% of deliveries are attended to by a trained personnel, whereas in Kerala state it is nearly 100%.

SECTION

15

Dermatology, Leprology and Sexually Transmitted Diseases

CHAPTER

41

General Considerations, Clinical Examination and Laboratory Investigations

Usha Vaidyanathan

Structure of the skin, Embryology, Microbial flora, Hair, Nail, Morphology of normal skin, History, Physical examination, Laboratory investigation, Differential diagnosis

INTRODUCTION

Dermatology is the branch of medicine which deals with the skin and its appendages.

STRUCTURE OF SKIN

The skin is a major organ in the body with a surface area of 1.8 m^2 in an adult, constituting up to 16% of the total body weight. Skin is composed of three layers, the epidermis, dermis and subcutaneous tissue.

Epidermis

The epidermis, which originates from ectoderm, is a stratified squamous epithelium about 0.1 mm thick. The thickness varies in different parts of the body. Its main function is to act as a protective barrier. Epidermis is mainly composed of keratinocytes, which produce a protein called keratin. The epidermis extends into the underlying dermis as finger like projections called rete ridges. Histologically, the epidermis consists of four layers.

1. *Stratum corneum* (horny layer) composed of sheets of overlapping flattened non-nucleated cornified cells.
2. *Stratum granulosum* (granular layer) composed of 2 to 3 layers of flattened cells containing coarse basophilic keratohyaline granules.
3. *Stratum spinosum* (prickle cell layer) composed of 5 to 8 layers of polygonal cells, which are interconnected by desmosomes (desmosomes are seen as prickles on light microscopy). *Langerhan's cells* are found mostly in this layer. These dendritic cells, derived from the bone marrow are the outermost sentinels of the cellular immune system. These cells are characterized by unique cytoplasmic organelle known as Birbeck granules, on electron microscopy.
4. *Stratum basale* (basal cell layer) composed of columnar cells, which are attached to the basement membrane by hemidesmosomes Melanocytes, seen as clear cells in between the basal keratinocytes, constitute about 5 to 10% of the basal cells. They arise from the neural crest. Melanocytes synthesize melanin and transfer it to neighboring keratinocytes via the dendritic processes. Melanin granules are uniformly distributed in the stratum corneum and they reduce the ultraviolet radiation penetrating the skin. In the deeper layers of the epidermis, the melanin granules form a protective cap over the outer part of the keratinocytes' nuclei.

Dermis

The dermis is a tough supportive connective tissue matrix, found immediately below the epidermis. Its thickness varies from 0.6 mm on the eyelids to about 3 mm on the palms and soles. It is made up of connective tissue fibers like collagen (70%) and elastin in a ground substance of glycosaminoglycans.

The thin upper layer of the dermis is called papillary dermis which interdigitates with the epidermal rete ridges. The deeper thick layer is

called reticular dermis with coarse bundles of collagen. The dermis also contains fibroblasts (which synthesize collagen, elastin and the ground substance), dendritic cells, mast cells, macrophages and lymphocytes.

The dermis is supplied with a rich network of blood vessels, lymphatics, nerves, eccrine glands, apocrine glands, sebaceous glands and hair follicles. Free sensory nerve endings are seen in the dermis, also extending to the epidermis. These nerve endings detect pain, itch and temperature sensation. There are specialized receptors called *Pacinian corpuscles* to detect pressure and vibration and Meissner's corpuscles in the skin of hands and feet, which detect touch.

Sebaceous glands are lipid-producing glands, distributed over the entire surface of the skin except the palms, soles and dorsum of feet. They are more numerous on the scalp and face. The major components of sebum are triglycerides, wax esters, squalene, cholesterol esters and cholesterol. Sebum which is present on the skin surface inhibits microbial proliferation.

Subcutaneous Layer

The subcutis is composed of adipose tissue (fat) of variable thickness and loose connective tissue.

EMBRYOLOGY

All constituents of human skin are derived from either ectoderm or mesoderm. The epithelial structures (epidermis, hair, nail, eccrine and apocrine glands and sebaceous glands) are derived from ectoderm. Melanocytes, nerves and special sensory receptors develop from neuroectoderm. The other elements in the skin (Langerhans' cells, macrophages, mast cells, fibroblasts, blood vessels, lymphatics, muscles, and adipocytes) originate from mesoderm.

Skin as an Immunological Organ

The epidermis acts as a physical barrier preventing the entry of micro-organisms into the body. The skin contains nearly all the elements of cellular immunity, except B-lymphocytes. Langerhans' cells and macrophages are important antigen presenting cells in the skin. They take-up the antigens from the skin surface, process it and present it to the T-lymphocytes along with the class II histocompatability (HLA-DR) molecule. Now the T-cells get activated and release a variety of proteins called lymphokines, like Interleukin (IL) 1,2,3 and 4, gamma interferon and B-cell differentiating factor (BCDF). Gamma interferon enhances the DR expression on the antigen-presenting cell, thereby increasing the T-cell response to antigen.

IL-2 binds to specific receptors on activated T-cells, giving rise to expansion of the activated clone of T-cells.

IL-4 and BCDF are important in the growth and maturation of antigen primed B-cells, which are involved in the production of antibodies. Thus the skin plays a major role in the recognition of an antigen or an allergen and the activation of the immune system.

MICROBIAL FLORA

A healthy normal skin is colonized by a variety of micro-organisms. Such true resident flora includes:

1. *Staphylococcus epidermidis, Staphylococcus aureus*—nose and perineum
2. *Micrococcus*—intertriginous areas and scalp
3. *Corynebacterium species*—axilla
4. *Propionibacterium species*—face, scalp, axilla
5. *Gram-negative organisms*—axilla, toe webs, nose
6. *Pityrosporum (fungi species)*—scalp
7. *Candida species*—intertriginous areas.

Resident flora prevent colonization by pathogenic organisms and also other commensal flora. Hydration of the skin is an important factor which determines the survival of the resident flora.

Normally vagina is sterile at birth. It is colonized by staphylococci, streptococci, and diptheroids within a few days. After puberty, lactobacilli predominate among the vaginal flora. They maintain an acidic pH of 4.5, which suppresses other bacteria, thereby improving local defence.

Functions of the Skin

The skin has many vital functions:

1. The skin acts as a mechanical barrier to protect the deeper structures from external injury and invasion by microbes.
2. The eccrine sweat glands and the blood vessels of the skin play a major role in temperature regulation.

3. The skin regulates the loss of body fluids by altering the rate of perspiration.
4. Melanin pigment protects the skin from the harmful effects of ultraviolet rays.
5. Skin acts as a major sensory organ receiving all superficial sensations.
6. Vitamin D synthesis occurs in the skin, on exposure to sun light.
7. Dendritic cells in the skin play a major role in immune surveillance.
8. Sebum has antimicrobial properties.

HAIR

Hairs are found over the entire surface of the skin except the glabrous skin of the palms, soles, glans penis and vulval introitus. The density of follicles is greatest on the face. The fetus is covered by fine, soft long hair called *lanugo* hair. Postnatal hair consists of soft, short unmedullated *vellus* hair over the body and large, coarse medullated terminal hair on the scalp and eyebrows. With the onset of puberty, androgens initiate the change of vellus hair to *terminal* hair in specific sites. The axillary and pubic hair in both sexes and the hair over the beard and moustache areas in males change into terminal hair.

New hair follicles are not formed after birth. Of the 100,000 hair follicles present on the average scalp, about 70 to 100 hairs are shed daily. Hair on the scalp grows at an average rate of 0.37 mm/day.

In men, scalp hair grows slower and hair on the trunk grows quicker than women. Hair growth occurs in a cycle of three phases.

Scalp hair cycle is as follows:

1. Anagen phase (growing phase)—3 to 10 years.
2. Catagen phase (involuting phase)—2 to 3 weeks.
3. Telogen phase (resting phase)—3 to 4 months.

Hair as an Indicator of Systemic Disease

The common hair disorders are hair loss (alopecia) and excess hair (hirsutism and hypertrichosis). Alopecia is classified as diffuse or localized and scarring and nonscarring.

Alopecia

Diffuse nonscarring alopecia is due to male pattern baldness (androgenic alopecia), hypothyroidism, hypopituitarism, hypoadrenalism and iron or zinc deficiency. Malnutrition causes dry brittle hair (pale or red in kwashiorkor).

Telogen effluvium is a condition where the hair follicles are set in a resting phase and shed together about 3 months later. It results from high fever, childbirth, surgery or other stress. Similarly cytotoxic drugs can arrest the hair growth abruptly leading to anagen effluvium.

Localized nonscarring alopecia is due to alopecia areata (Fig. 41.1), hair pulling, traction, dermatophyte infection and secondary syphilis.

Scarring alopecia is uncommon and is associated with morphea, lichen planus (Fig. 41.2), tertiary syphilis, radiation, trauma and others.

Excess Hair

Hypertrichosis is excessive terminal hair growth in a nonandrogenic distribution. It is usually due to



Fig. 41.1: Alopecia areata



Fig. 41.2: Lichen planus scalp-scarring alopecia

systemic illnesses like malignancy, porphyria cutanea tarda, anorexia nervosa and drugs like minoxidil, phenytoin and cyclosporin A.

Hirsutism is the occurrence of a male pattern of terminal hair, in a female. Though commonly idiopathic, polycystic ovaries and other endocrine disorders can cause hirsutism.

The vellus hairs are converted to terminal hairs in androgen sensitive hair follicles of the beard area, upper lip, chin, chest, upper and lower back, upper and lower abdomen, arm, forearm, thigh and leg.

NAIL

Nail is a phylogenetic remnant of the mammalian claw. It consists of a nail plate made up of hard keratin, which is derived from the nail matrix at the base of the nail. It protects the finger tip, facilitates grasping and tactile sensitivity in the finger pulp. The cuticle is an extension of the horny layer of the epidermis on to the nail plate. Finger nails grow at a rate of 0.1 mm daily and toe nails grow at about one-third to one-half that rate.

Nail in systemic disease: Nail changes may indicate an underlying systemic disease. Transverse grooves called Beau's lines can occur due to any severe systemic illness that affects the growth of the nail matrix. Brittle nails are common with chronic irritation due to water and detergents, iron deficiency and others.

White spots of the nails are due to trauma to nail matrix. Certain drugs cause color changes in the nail (yellow discoloration by tetracycline, black transverse bands by cytotoxic drugs, white transverse bands due to heavy metal poisoning, blue color by antimalarials, brown color by chlorpromazine and gold). Pseudomonas infection can cause a blue-green discoloration. Nails become white due to hypoalbuminemia and yellow due to jaundice. Splinter hemorrhages, seen as red streaks may occur due to infective endocarditis and trauma.

Nail involvement in common dermatoses:

1. *Tinea unguium:* Caused by dermatophytes. Onycholysis (separation of nail plate from nail bed), dystrophy and subungual hyperkeratosis. Starts at the distal end of nail.
2. *Chronic paronychia:* Caused by *Candida albicans.* The cuticle is damaged, proximal nail fold is swollen, with dystrophic and discolored nails. Acute paronychia is usually bacterial (staphylococcal).
3. *Psoriasis:* Pitting, onycholysis (Fig. 41.3), subungual hyperkeratosis, nail thickening, brown discoloration, oil drop sign.
4. *Lichen planus:* Nail thinning, longitudinal grooves, pterygium.
5. *Eczema:* Coarse pitting, transverse ridging and dystrophy.



Fig. 41.3: Psoriasis of nails. Note the destruction and separation of the nail plate

MORPHOLOGY OF NORMAL SKIN

A healthy normal skin is smooth, soft, uniformly pigmented, neither dry nor oily and capable of appreciating normal sensations. As age advances several changes take place in the skin. These include loss of elasticity, dryness, wrinkling, loss of oiliness, atrophy and appearance of hyperkeratotic and pigmented spots. Thinning and greying of terminal hairs occur. In those with a genetic predisposition to baldness the terminal hair of the scalp is converted to vellus hair.

HISTORY

Since the skin is the tissue most obvious to the patient and others, the psychological and social problems caused by skin diseases are out of proportion to their structural and functional severity. Many systemic diseases such as exanthemata and hemorrhagic diseases produce skin lesions as their

heralding manifestations. On the other hand several skin diseases like exfoliative dermatitis produce systemic effects. All these factors have to be taken into consideration before proceeding with the examination. The diagnostic process includes history, physical examination and investigations.

The dermatologic history begins with the patient's *presenting complaint.* It is essential to find out when, where and how the problem started, what the initial lesions looked like and how they evolved and extended. For example, psoriasis often starts on the back of the elbow whereas scabies often affects the interdigital skin folds.

Associated symptoms should be enquired, like itching, nocturnal aggravation of itching (scabies), pain (furuncle, herpes zoster), loss of sensation as in Hansen's disease or asymptomatic (nevus, lichen nitidus). Systemic symptoms should also be noted.

Remissions and relapses can occur in certain conditions like psoriasis, atopic dermatitis and allergic contact dermatitis.

Aggravating factors should be enquired into:

- Sunlight exacerbates photodermatitis
- Seasonal variations (ichthyosis worsens in winter, Darier's disease worsens in summer, psoriasis improves in summer)
- Allergic disorders may be aggravated by allergens in diet or environment
- Emotional disturbances aggravate many dermatological disorders like psoriasis and neurodermatitis.

Past history: History of similar illness in the past gives helpful clue to the diagnosis of allergic disorders, psoriasis, photodermatitis and others. History of diabetes, hypertension and bronchial asthma should be enquired.

Diabetics are more prone to candidal infections, bacterial infections with *Staphylococcus aureus*, erythrasma and serious infections like necrotizing fasciitis and pseudomonas infections. Acanthosis nigricans, scleredema (thickening of skin of back and neck) and Kyrle's disease especially in diabetics with chronic renal failure. Kyrle's disease (Fig. 41.4) presents as follicular and extrafollicular papules with central keratotic plug and may form verrucous plaques, commonly on the legs and arms.

Necrobiosis lipoidica diabeticorum (asymptomatic red papules and plaques which resolve with yellowish atrophic plaque that may ulcerate, on the pretibial skin) is also associated with diabetes. Drugs like sulphonyl urea, used in diabetes, can cause photosensitivity. Drugs used for hypertension, for example, beta blockers, may aggravate psoriasis.

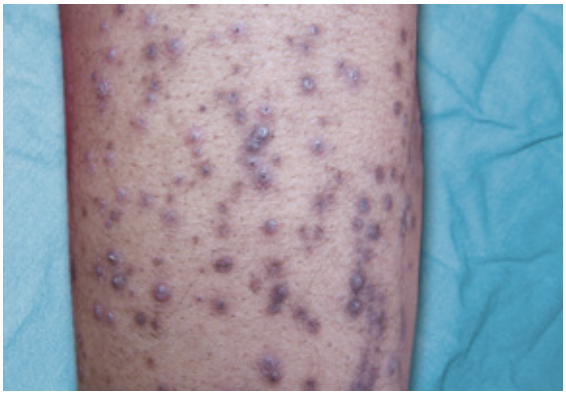


Fig. 41.4: Kyrle's disease—keratotic papules with central plugs

Family history: A positive family history may be obtained for diseases such as psoriasis. Atopic dermatitis, asthma and other allergic diseases may occur in several family members. Autosomal recessive diseases like xeroderma pigmentosum and lamellar ichthyosis may reveal consanguinity among the parents. Several members of the family, especially children may show signs of scabies.

Drug history: Treatment received (both prescribed and self-administered, topical and systemic drugs) and its effect has to be enquired. Partially treated lesions, especially with topical steroids, change their morphology considerably. Cosmetics can also cause dermatitis and their use has to be asked for specifically.

Personal history: This is particularly important in cases of suspected contact dermatitis and several other skin disorders. The details of occupation, habits, hobbies, diet, cosmetics, clothes and home surroundings help to diagnose many of them straight away.

PHYSICAL EXAMINATION

The whole skin surface should be examined under proper illumi nation, preferably natural light. Hair, nails, palms, soles and mucous membranes of the

mouth, genitalia, nose and eyes should be examined.

The morphology of the individual lesion, configuration and distribution of lesions should be noted.

Morphology

Skin lesions are classified as primary or secondary. Primary lesions arise *de novo* from the skin. Secondary lesions arise secondary to the primary lesions.

Primary Lesions

Macule: An alteration of colour of the skin up to 1 cm in diameter is called a macule. It is flush with the surface, e.g. hypopigmented macule. (Fig. 41.5) and depigmented macule (Fig. 41.6), hyper pigmented macule.

Patch: A macule more than 1 cm is called a patch. Total absence of pigments leads to vitiligo (Fig. 41.7).

Papule: A solid elevated lesion up to 1 cm in diameter is a papule. (Figs 41.8 and 41.9). The surface of the papule may be flat-topped, dome shaped, verrucous, filiform (Fig. 41.10) or umbilicated.

Plaque: A solid elevated lesion larger than 1 cm is called a plaque (Fig. 41.11).

Nodule: A nodule is a solid swelling situated within the skin. It is better felt than seen.

Vesicle: It is an elevated lesion containing clear fluid up to 1 cm in diameter (Fig. 41.12).

Bulla: Fluid filled lesion more than 1 cm is called a bulla (Fig. 41.13).

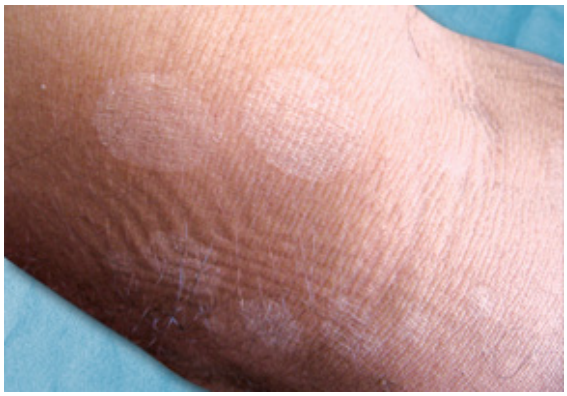


Fig. 41.5: Macules of pityriasis versicolor



Fig. 41.7: Depigmented patch of vitiligo



Fig. 41.6: Depigmented macule—vitiligo



Fig. 41.8: Minute papules of lichen nitidus

Pustule: It is an elevated lesion containing pus (Figs 41.14 and 41.15). Usually pustules are small and less than 1 cm in diameter.

Abscess: It is a large collection of pus underneath the skin.

Wheal: It is an evanescent, edematous skin lesion. It may be erythematous, skin colored or pale (Fig. 41.16).

Purpura: This is a circumscribed hemorrhagic lesion up to 1 cm in diameter, which is flush



Fig. 41.9: Violaceous flat topped lesions of lichen planus



Fig. 41.12: Herpes simplex infection—grouped vesicles nasolabial fold



Fig. 41.10: Filiform wart



Fig. 41.13: Vesicles and bullae in contact dermatitis



Fig. 41.11: Plaque psoriasis



Fig. 41.14: Follicular pustule

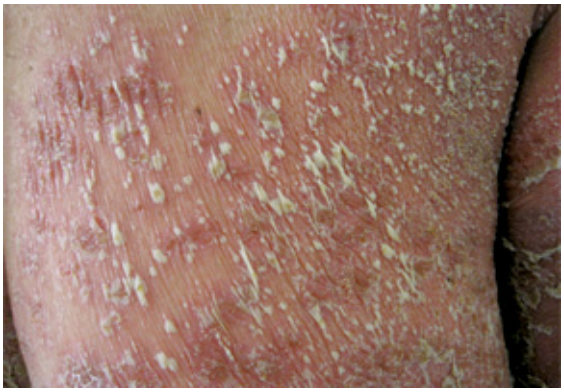


Fig. 41.15: Sterile pustules of psoriasis

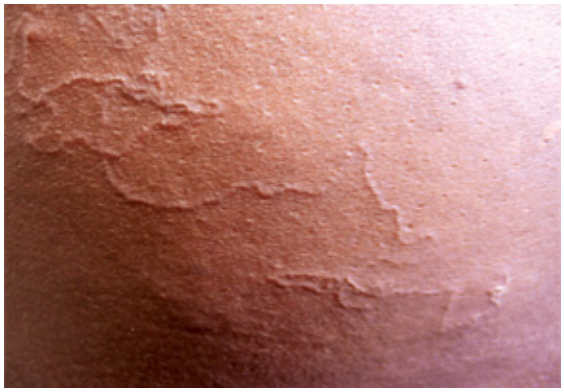


Fig. 41.17: Tunnel formed by larva migrans



Fig. 41.16: Urticaria causing wheal (arrow)



Fig. 41.18: Acne comedones (arrow)

with the surrounding skin or mucous membrane. The lesion does not blanch on pressure. Palpable purpura is a feature of Henoch-Schönlein purpura. Larger lesions are called ecchymoses and pin-point lesions are called petechiae.

Cyst: A cyst is a sac that contains liquid or semisolid material.

Sclerosis: Sclerosis is hardening of the skin due to dermal or subcutaneous edema, cellular infiltration or increased collagen, e.g. scleroderma.

Special Primary Lesions

Burrow: It is a tunnel produced by the movement of a parasite within the tissue. It is seen as a straight or zig-zag line that may be grayish. These are seen in scabies and larva migrans (Fig. 41.17).

Comedones: These are dark plugs seen inside the opening of a hair follicle (Fig. 41.18). This is the primary lesion in acne vulgaris. It is also seen in people using cutting tools or lubricating oils under high pressure.

Telangiectasia: Persistent dilatation of the post-capillary venules is called telangiectasia.

Target lesion: (Iris lesion) has a central vesicle or purpura, surrounded by a zone of edema and an outer ring of erythema. Classically seen in erythema multiforme.

Secondary Lesions

Scales: Visible dry exfoliation of the superficial layers of the epidermis is called scaling.

Crust: This is formed of dried up discharges such as serum, pus or blood.

Erosion: Loss of superficial skin leaving a raw area is called erosion (Fig. 41.19). This is seen in pemphigus when the bulla ruptures and in acute eczema.

Ulcer: Loss of whole thickness of skin due to infection, ischemia or necrosis leads to ulceration.



Fig. 41.19: Erosions, crusting and scaling in contact dermatitis



Fig. 41.21: Atrophy of skin due to long-term topical steroid



Fig. 41.20: Lichenification—note the exaggeraged skin marking (arrow)



Fig. 41.22: Annular plaque of tinea faciale

Fissures: Fissures are linear cracks exposing the deeper aspects of the skin.

Lichenification: The skin markings become prominent. This is usually associated with pigmentation and thickening (Fig. 41.20).

Excoriation: Excoriation is superficial denudation of the skin covered by black crust.

Atrophy: Skin is thin, shiny and wrinkled. (Fig. 41.21). Atrophy can occur in the epidermis, dermis or the subcutis.

Scar: Scar is an alteration in the appearance and texture of the skin which heals in areas of tissue destruction. A depressed scar is an atrophic scar.

Excessive scar tissue occurs in keloids and hypertrophic scar.

Keloids originate at the site of injury or even without an injury, example, presternal region. It can extend beyond the site of injury in a claw like fashion and continue to increase in size for decades or may remain stable. It may be familial.

Hypertrophic scars originate at the site of injury only. It is confined to that site and does not extend beyond the original injury. It tends to regress with time and flatten. There is no familial susceptibility.

Combination of Lesions

More than one type may be combined in a single lesion. A vesicle or pustule can occur on top of a macule or papule. The various combinations noted are maculovesicle, maculopapule, papulovesicle, papulopustule, papulosquamous, and so on.

Configuration of Lesions

After noting the type of skin lesion, see whether the lesions tend to take any particular pattern.

Annular lesions (ring-like) are seen in dermatophyte infection (Fig. 41.22), granuloma



Fig. 41.23: Epidermal nevus—note the linear lesions

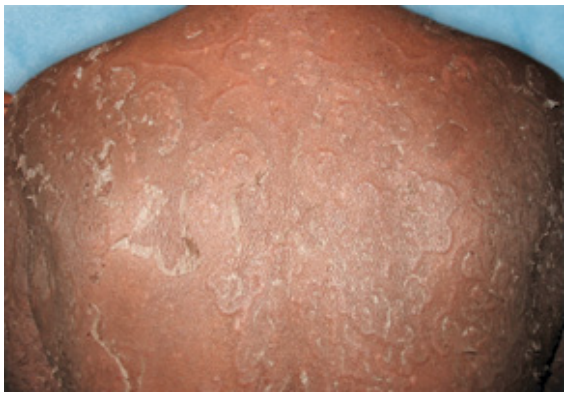


Fig. 41.24: Gyrate pattern of lesions in erythema gyratum repens

annulare, and annular erythema. Grouping of lesions is seen in herpes simplex (See Fig. 41.12), herpes zoster and dermatitis herpetiformis. Linear pattern is seen in some types of congenital nevi (Fig. 41.23), lichen striatus, linear morphea and others.

Arciform lesions occur as incomplete rings or C-shaped lesions. These are seen in some cases of secondary syphilis. Gyrate pattern (circular or spiral) is seen in erythema gyratum repens (Fig. 41.24), a dermatological manifestation of internal malignancy.

Zosteriform pattern (girdle pattern) is seen in herpes zoster, and some forms of nevi, vitiligo and morphea which follow a dermatomal distribution

Generalized lesions are seen in specific patterns like 'S' shaped, linear and whorls in some verrucous epidermal nevus and incontinentia pigmenti. These do not follow segmental pattern (Fig. 41.25).

Koebner phenomenon (isomorphic effect): This is the phenomenon in which similar lesions can be reproduced by physical trauma. For example,



Fig. 41.25: Lesions along Blaschkos lines in epidermal nevus

lesions of lichen planus develop linearly along scratch marks, injuries or operation scars.

Distribution of Lesions

Elicit whether the lesions are generalized or localized (Fig. 41.26), bilateral or unilateral and symmetrical or asymmetrical. Look for areas of greater involvement, e.g. sun-exposed areas and sparing of any region (Fig. 41.27). An extensor distribution is common in psoriasis and flexor distribution in lichen planus. Scabies lesions occur in a particular distribution on inter digital spaces of fingers (Fig. 41.28), medial wrist, elbows, anterior axillary fold, nipples in females and genitalia in males, completing an imaginary circle called "circle of Hebra".

Though dermatological diagnosis is largely dependent on inspection, palpation of the skin helps in certain situations like assessing the texture, consistency, depth of lesions and tenderness.

Examine the mucous membranes of the mouth and genitalia for discoloration, erosion or ulceration. Examine the hair for its color, texture and alopecia. Examine the nails for pitting, ridging, discoloration, dystrophy, thickening and subungual keratosis.

Systemic Examination

After the dermatological examination an appropriate general examination and systemic examination should be performed.



Fig. 41.26: Allergic contact dermatitis to bangle—well demarcated and localized



Fig. 41.28: Scabies Lesions on interdigital space (arrow)



Fig. 41.27: Photo distribution—note the sharp demarcation between covered and exposed parts (arrow)

Common Clinical Tests

Special tests are performed to elicit diagnostic signs.

Gruttage

Scraping the surface of a psoriatic lesion in a non-hairy area with a glass slide releases silvery scales as if one is scratching the surface of a candle. This is called "candle grease" sign. Once all the scales are removed a thin membrane is exposed and on removing this membrane multiple pinpoint bleeding is seen. This is called *Auspitz's sign* and it is pathognomonic of active psoriasis. It may not be positive in a healing lesion.

Nikolsky's Sign

In cases of active pemphigus vulgaris, if tangential pressure is applied with the thumb on a normal looking skin over a bony prominence as on the medial surface of the tibia, the skin gets separated from the underlying wider area than on the vesicles themselves. This test may be positive in toxic epidermal necrolysis and some forms of epidermolysis bullosa.

Bulla Spread's Sign

Pressure is applied over the edge of a bulla. The fluid will spread to the surrounding normal looking area. The basis is the same as that of *Nikolsky's sign*.

Dermographism

Stroking the skin with a blunt object produces an exaggerated triple response, the red line, flare and edema. This is positive in some types of urticaria and also in mastocytosis. White dermographism is the one in which pallor develops instead of the flare. This is a feature of atopy.

Darrier's Sign

Rubbing the macular lesions in urticaria pigmentosa induces a wheal.

Diascopy

The lesion is pressed with a flat transparent glass slide. This helps to differentiate between purpura and erythema. In purpura, the lesion does not blanch, but in erythema the lesion blanches on pressure and the color returns on releasing the pressure. In lupus vulgaris a yellowish brown apple jelly appearance may be seen on diascopy.

Wood's Lamp

It emits long wavelength ultraviolet radiation (360 nm) which will cause hair and skin to fluoresce. The examination should be done in a dark room.

1. Hypo and hyperpigmentation are enhanced with wood's lamp. Epidermal pigmentation of melasma appears darker and dermal pigmentation is not enhanced under wood's lamp.
2. Erythrasma, caused by *Corynebacterium minutis simum* produces a coral-red fluorescence.
3. Tinea capitis caused by microsporum species is an ectothrix infection that occurs outside the hair shaft and gives a bright green fluorescence on wood's lamp. Trichophyton species causing endothrix infection do not fluoresce.

Intradermal Test

This is done to detect immediate type of allergy such as anaphylaxis and urticaria. 0.05 ml of suspected antigen is injected intradermally on the flexor aspect of the forearm. Several antigens can be injected simultaneously in different parts. A control with 0.05 ml of normal saline or the diluent should also be given on the other forearm. The test is read after 30 minutes. Increase in diameter of the wheal and erythema are noted. If the diameter of the wheal is more than 1½ times the control, the test is considered positive.

Scratch Test

It is similar to intradermal test. Here a drop of antigen is placed on the forearm and two scratches are made with a needle through the solution in the epidermis. Development of a wheal at the site of scratch is taken as positive. The patient should not have any active lesion and should not be on antihistamines or steroids at the time of test.

Patch Test

This is done in cases of suspected allergic contact dermatitis. The antigen solution is applied on 0.5 cm^2 lint and pasted on the forearm or back and secured with adhesive plaster for 48 hours after which the reaction is noted for erythema, edema, or vesicles. Several antigens can be applied simultaneously. The antigens are applied in low concentrations which will not cause direct irritation when kept under occlusion for 48 hours.

Photo-Patch Test

When photo contact dermatitis is suspected, the patch test is done in the usual way. If there is no reaction after 48 hours, the test site is exposed to sunlight for 30 minutes and occluded again for a further 48 hours and then read.

LABORATORY INVESTIGATIONS

Demonstration of fungus by microscopy: In cases of dermatophytosis scrapings should be taken from the active margin of the lesions. In cases of suspected candida infection scraping should be taken from the white sodden epidermis. In tinea versicolor scrapings should be taken from the surface of the lesions. The scraped material is placed in a drop of 10% potassium hydroxide solution, with a cover slip and kept for 10 minutes, before microscopy. Warming the slide separates the keratin early and brings out the fungal hyphae better. Septate branching hyphae are seen in dermatophyte infection. Short nonbranching slightly curved hyphae and rounded spores are seen in tinea versicolor. Yeasts and pseudohyphae are seen in Candida infection. Fungus can be demonstrated in nail clippings after soaking them at least for 1 hour in potassium hydroxide (preferably overnight). Fungal hyphae and spores can be demonstrated in the hair plucked from affected sites. Fungus can be cultured in Saboraud's medium. Scrapings from lesions of crusted scabies reveal *Sarcoptes scabiei* after similar preparation.

Tzank Test

This is done in cases of vesiculobullous disorders. The top of the bulla is removed with scissors and the fluid is wiped off. A smear is made on a glass slide with scrapping from the base of the bulla, fixed and stained with Leishman's stain.

Acantholytic cells which are round or oval cells with central nucleus, perinuclear halo and condensation of the cytoplasm at the periphery are seen in pemphigus vulgaris and benign pemphigus of Hailey and Hailey. Multinucleated giant cells are seen in viral bullae. Polymorphs and eosinophils may be seen in dermatitis herpetiformis and bullous pemphigoid respectively.

Gram Stain of Pus

This is done to differentiate pyogenic infections from sterile pustules of pustular psoriasis and subcorneal pustular dermatoses.

Microscopic Examination of Hair

Portions of the hair can be examined on a glass slide after covering them with a drop of cedar wood oil and applying a cover slip on top. Conditions such as piedra, trichorrhexis nodosa and pili torti can be diagnosed by microscopy.

Skin Biopsy

A well-developed lesion should be selected for biopsy except in vesiculobullous diseases in which the early lesion should be taken *in toto* with some surrounding skin.

DIFFERENTIAL DIAGNOSIS OF COMMON DERMATOLOGICAL PROBLEMS

Generalized Itching (Syn: Pruritus)

Skin Diseases

Dry skin, scabies, drug eruptions, urticaria, dermatitis herpetiformis.

Systemic Diseases

Diabetes mellitus, uremia, anemia, liver diseases, obstructive jaundice, internal malignancy.

Localized Itching

Dermatophytosis, neurodermatitis, atopic dermatitis, pediculosis, papular urticaria, lichen planus.

Differential Diagnosis of Primary Skin Lesions

1. Hypopigmented macules	Pityriasis alba, tinea versicolor, leprosy, early vitiligo, nevus anemicus and nevus achromicus
2. Hyperpigmented macules	Freckles, fixed drug eruption, macular lichen planus, pigmented nevus, urticaria pigmentosa, heavy metal poisoning, e.g. arsenic, mercury
3. Erythematous macule	Exanthema, drug reactions
4. Asymptomatic papules	Secondary syphilis, pityriasis rosea, xanthoma, wart, molluscum contagiosum, leprosy
5. Vesicles	Herpes simplex, herpes zoster, chickenpox, irritant dermatitis, drug induced
6. Vesicles and bullae	Pemphigus, dermatitis herpetiformis, pemphigoid, toxic epidermal necrolysis, epidermolysis bullosa, bullous impetigo, congenital syphilis, insect bites
7. Pustules	Folliculitis, pustular miliaria, pustular psoriasis, subcorneal pustular dermatosis
8. (a) Annular lesions	Tinea corporis, granuloma annulare, annular erythema, secondary syphilis, annular lichen planus, pityriasis rosea
(b) Linear lesions	Nevus, scleroderma, lichen striatus, lichen planus
9. Koebner phenomenon	Psoriasis, lichen planus, lichen nitidus, vitiligo, warts
10. Mucous membrane lesions	Lichen planus, leukoplakia, candidiasis, secondary syphilis, erythema multiforme, malignancy

CHAPTER

42 Clinical Methods in Leprology

Usha Vaidyanathan

History, Physical examination, Investigations

INTRODUCTION

Leprosy is one of the major chronic granulomas affecting large population groups in developing countries. Leprology has developed as a sub-speciality. The Government of India has accepted leprosy as a major disease of national importance and initiated the leprosy control programme. Since the introduction of multidrug therapy (MDT), the global prevalence of leprosy has fallen dramatically. Currently estimated total number of cases in the world stands at 2,13,036 in early 2009, compared to 10 to 12 million in 1985. In India, the prevalence of leprosy has been reduced from 52/10,000 in 1981 to 5.8/10,000 by March 1997. In July 2006, prevalence in India has fallen to 0.88/10000. However, sporadic cases of leprosy will occur for many more years and clinical suspicion should be strong in order to make early diagnosis.

The manifestations of leprosy vary widely. The clinical spectrum includes a single transient lesion or mononeuritis at one end and severe involvement of the skin, mucous membranes, vital organs and mononeuritis multiplex at the other end. The clinical presentation in a given patient depends on the immune status of the individual. If the immunity is good, he develops lesions of tuberculoid spectrum and if the specific immunity is poor, he develops lepromatous lesions and in between comes the borderline spectrum. Thus, the clinical spectrum varies from tuberculoid (TT) -borderline tuberculoid (BT)-borderline borderline (BB)-borderline lepromatous (BL)-lepromatous leprosy (LL).

Tuberculoid Leprosy

A typical tuberculoid lesion is usually single (may be 2–3), erythematous or coppery plaque, has an irregular dry surface, raised well-defined edges and central flattening. There is loss of sensation, loss of hair and loss of sweating. Thickened nerves may be palpable in the vicinity of the lesion.

Borderline Spectrum

This is the most common and immunologically unstable form of leprosy. Lepra reactions and crippling deformities from nerve damage are more common. Borderline leprosy presents as hypo-pigmented patches, erythematous or coppery plaques, and annular or bizarre lesions.

Borderline Tuberculoid

Patches of Borderline Tuberculoid (BT) (Fig. 42.1) are only a few in number, partly well-defined and anesthetic (not as complete as in TT). The surface is dry. Bacilli are scanty or absent.

Borderline Borderline

Large annular or bizarre lesions (Fig. 42.2) with ill-defined edges and bacilli are always present.

Borderline Lepromatous

Near the lepromatous end of spectrum, the number of macules increases (Fig. 42.3), they are less well-defined and less anesthetic, and more shiny.

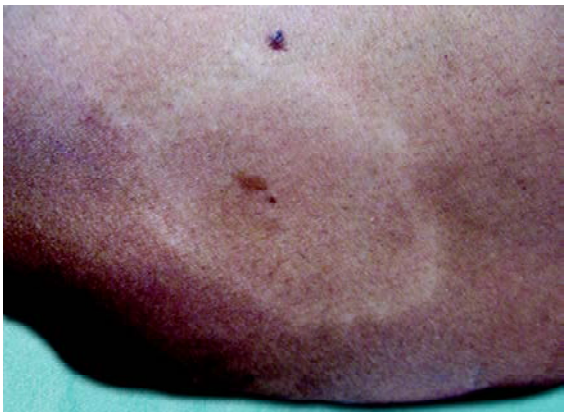


Fig. 42.1: Asymptomatic patch of leprosy (BT)



Fig. 42.2: Leprosy—large bizarre lesions (BB)



Fig. 42.3: Leprosy—multiple lesions of BL

They contain numerous lepra bacilli. Nasal scrapings are negative. Nerve thickening (bilateral and asymmetrical) with or without muscle paralysis and anesthesia in the area of distribution of affected nerves are common.

Lepromatous Leprosy

Manifests as small, shiny, numerous, hypopigmented or coppery macules with ill-defined edges. There is no sensory impairment. Papules and nodules may also occur. The lesions are bilaterally symmetrical. They are distributed mainly over the face, arms, buttocks, legs and also the trunk. Warmer areas like axilla, groin, perineum and hairy scalp are spared. Nerve involvement occurs only late in the disease and are bilaterally symmetrical. Bilateral glove and stocking anesthesia occurs in the limbs. Systemic involvement is common.

Indeterminate Leprosy

Indeterminate leprosy is an immunologically unstable form of leprosy commonly seen in children. It presents as a single (sometimes more) hypopigmented or erythematous, ill-defined or well-defined *macule* (never raised), commonly over the covered areas of the body. Loss of sensation and nerve thickening may or may not be present. The lesions heal spontaneously in 70% of patients. The rest 30% progress to a determinate type of leprosy, more commonly to lepromatous spectrum.

Cardinal Signs of Leprosy

1. Alteration of sensation in a lesion characteristic of leprosy, or in an area supplied by one or more of the peripheral nerves.
2. Thickening and/or tenderness of peripheral nerve trunks.
3. The finding of acid-fast bacilli in smears from skin lesions or normal looking skin.

At least two out of these three signs must be present for a diagnosis of leprosy.

Lepra reactions, which occur during the course of leprosy cause many symptoms that often compels the patient to seek medical advice. There are three types of reaction.

Type I lepra reaction (delayed hypersensitivity reaction) is common in borderline leprosy. An acute exacerbation of existing lesions (erythema, edema, tenderness) or occurrence of new lesions, edema of hands and feet and acute neuritis are the features of Type I reaction.

Type II lepra reaction (immune complex mediated) is seen in lepromatous leprosy. It is characterized by *erythema nodosum leprosum* (ENL), which presents as erythematous, small nodules or plaques, bilaterally symmetrical, tender, warm and evanescent (lasts for only 2–3 days). ENL lesions are commonly seen over the face, arms and thighs. Other features include fever, malaise, joint pain, iritis, epididymo-orchitis, neuritis, epistaxis, proteinuria and bone pain.

Type III lepra reaction (Lucio phenomenon) occurs in Lucio leprosy, which is rare in India.

HISTORY

Important points to note in history are:

1. When, where and how the lesions started
2. The evolution of lesions
3. Onset (whether insidious or sudden)
4. Any symptoms (leprosy lesions are usually asymptomatic). Details of hyperesthesia, paresthesia or anesthesia of any part should be elicited. Anesthesia leads to blistering, ulceration and loss of tissues, particularly fingers and toes
5. Sudden or insidious onset of muscle weakness or paralysis
6. Nasal symptoms (nasal stuffiness, crust formation, blood stained discharge), bilateral pedal edema—these are features of early lepromatous leprosy.
7. Systemic involvement is common in lepromatous leprosy. These include fever, iridocyclitis, epididymo orchitis, renal involvement and others. These aggravate during lepra reactions.

PHYSICAL EXAMINATION

In addition to a routine examination of the skin, superficial sensations should be looked for. The most obvious abnormalities are diminution or loss of sensations of temperature, touch and pain. It should also be noted whether there is infiltration of the face, ear lobes or other parts of the skin.

Specific points to note in order to classify the spectrum are:

1. Number of lesions increases through the spectrum from TT to LL
2. Size of lesions is bigger in borderline and decreases in LL
3. Surface of lesions is dry in TT and shiny in LL
4. Loss of sensations in lesions is marked in TT, but not so in LL
5. TT lesions are bacteriologically negative, whereas LL lesions team with lepra *Bacilli*
6. *Lepromin test*, which is strongly positive in TT, becomes negative in BB, BL and LL (This is seldom done in practice).

Examination of Peripheral Nerves

The following nerves should be inspected and palpated for thickening, tenderness and nodularity which suggest nerve abscess:

1. Supratrochlear and supraorbital nerves on the forehead
2. Zygomatic branch of the facial nerve on the face
3. Great auricular nerves over the sternomastoids
4. Supraclavicular nerves over the clavicle
5. Radial nerves in the radial grooves in the arms
6. Ulnar nerves behind the medial epicondyles
7. Lateral cutaneous nerve in the anatomical snuffbox
8. Median nerves in the middle of the flexor aspect of the wrists
9. Common peroneal nerves lateral to the head of the fibulae. Finger should be rolled upwards and forwards
10. Sural nerves in the middle of the posterior aspect of the lower part of the legs
11. Superficial peroneal nerves in the lower third of the lateral aspect of the legs and crossing in front of the ankle to the dorsum of the feet
12. Posterior tibial nerves behind the medial malleoli
13. Any cutaneous nerve near a skin patch.

Sensation should be tested over the cornea, hands and feet. Deformities such as claw hand and foot drop should be looked for. Muscle power should also be tested in the distribution of the affected nerves.

INVESTIGATIONS

Slit Skin Scraping for AFB (Skin Smear)

In all cases of suspected leprosy, skin smears should be examined to demonstrate *Mycobacterium leprae*. In positive cases this should be

repeated every 6 months to assess the progress. It should ideally be taken from 4 sites, one from the patch, both the ear lobes and normal looking skin.

Hold the skin or the ear lobe firmly between the thumb and the index finger. Make a slit 0.5 cm in length. If there is any bleeding, wipe off the blood and then scrape out some tissue with a pointed scalpel, make a smear, fix it over the flame, stain by modified Ziehl-Neelsen's method. Examine under the oil immersion microscope. Note the presence and morphology of the acid fast bacilli, whether they are uniformly stained, fragmented or granular and also the approximate number of bacilli in an average field.

Live and dead bacilli should be differentiated to know the progress during treatment. Live bacilli are solid rods and stain uniformly. Dead bacilli are fragmented or granular and stain irregularly. The percentage of solid stained bacilli, calculated after examining 200 red-staining elements lying singly is called morphological index (MI). This gives valuable information on whether the disease is active or not. MI reduces with treatment and falls to zero in 4 to 6 months.

The density of bacilli in smears is known as the bacteriological index (BI) and includes both live and dead bacilli. BI is high in lepromatous and few or no bacilli in TT. BI remains the same for 12 months and then steadily falls over the next 5 to 10 years.

Skin Biopsy

Biopsy is indicated for confirmation of diagnosis in cases of doubt and also for proper classification of the type of leprosy.

Lepromin Test

It is an intradermal test in which 0.1 mL of antigen is injected intradermally on the forearm. The Fernandez reaction is read after 48 hours and the Mitsuda reaction after four weeks.

The Fernandez reaction is a delayed type of hypersensitivity reaction to the bacillary antigen. The mitsuda reaction is indicative of cell-mediated immune response and is more valuable in assessing the immune status. Lepromin test is not commonly performed, but is done for research purposes rarely at times.

CHAPTER

43

Sexually Transmitted Diseases: Genitourinary Medicine

Usha Vaidyanathan

Special points in interrogation, Physical examination, Investigations

Recording of history and physical examination follows the general pattern. As these diseases are sexually transmitted, they carry social stigma and the patients are usually hesitant to divulge the correct history due to fear of ostracization. Hence, these patients should be given enough privacy and confidence.

Medical fraternity should change their attitude towards these patients and be kind and courteous to them. They should not be discriminated upon. They deserve all respect and hospitality.

Suppressing the illness causes harm to the patient and favors spread to others. Therefore, the aim of the doctor should be to cure all cases and trace all contacts from the index case. It should be remembered that the same patient may suffer from multiple STDs.

SPECIAL POINTS IN INTERROGATION

Sexual exposure: History of premarital, extramarital or marital exposure, the frequency of exposures, the type of sex practiced (genital, oral, anal, etc.) and the date of last exposure should be asked for.

Nature of sexual partner: The nature of the sexual partner such as prostitute, call girl, casual acquaintance, neighbor, relative, foreigner, etc. and also the place of exposure are important. The sexual practices-whether heterosexual, bisexual or homosexual should be ascertained.

Personal history: Marital status and occupation should be asked for. In females with suspected late syphilis obstetric history should be recorded. If the patient had only one exposure prior to the onset, the incubation period can be inferred correctly. Attempts should be made to trace all the contacts so that they can be summoned and treatment offered. Enquire into the past occurrence of STD and treatment taken by the patient and the sexual partner.

Presenting complaint: Males with urethritis complain of pain during micturition and discharge per urethra.

PHYSICAL EXAMINATION

In males examine the genitalia, look for any discharge. Retract the prepuce, examine the glans penis, coronal sulcus and the undersurface of the prepuce. If ulcers are present note their number, size, shape, surface and surrounding area. With gloved hands, palpate the ulcer for tenderness and induration. Examine the scrotum and testes. Lift the scrotum and examine its under surface also. Examine the anal region for discharge, ulcers, moist papules or verrucous lesions.

Note the nature of the discharge, whether it is purulent (gonorrhea), mucopurulent, mucoid (non-specific urethritis), or blood stained.

In females with history of excessive vaginal discharge, the nature of the discharge—whether it is purulent (gonococcal), white and curdy (candidiasis) or yellowish and frothy (trichomoniasis), should be determined. If ulcers are present, their onset and presence of any vesicles or trauma prior to the ulcer should be ascertained.

Syphilitic chancre is usually single, indolent, painless and indurated with bilateral painless lymphadenopathy of rubbery consistency.

The ulcers of chancroid are usually multiple, shallow, painful, sharply circumscribed with ragged undermined edges, floor covered with vascular granulation tissue and bleeds easily on touch. Usually unilateral, tender, matted, lymphadenopathy occurs in a few days to weeks and it suppurates to form a unilocular abscess.

In lymphogranuloma venereum (LGV), the primary lesion is small, herpetiform, painless, nonindurated, usually single and frequently unnoticed by the patient as it heals very quickly. Lymphadenopathy follows in a few weeks, which is unilateral (in two-thirds of cases), tender and matted. Enlargement of nodes above and below the inguinal ligament gives a characteristic grooved appearance called the 'sign of the groove'.

Examination of Lymph Nodes

The inguinal, external iliac, epitrochlear, posterior cervical and axillary lymph nodes should be examined.

Mucous membrane of the mouth and throat should be examined for mucus patches, erosion or ulcers. Skin lesions, alopecia, ocular lesions and hepatomegaly should be positively looked for.

Examination of Females

Lithotomy position is ideal for examining the genitalia. The external genitalia, vagina, urethra and cervix should be examined. Except in virgins with intact hymen speculum examination should be done. Further examination is similar to that in males.

Proctoscopy

This should be done and any discharge, ulcer, growth or stricture should be looked for. If there is discharge it should be examined for gonococci, ameba, and other organisms.

Prostatic Massage

It is indicated in males with chronic prostatitis for diagnosis as well as for therapy. The gloved index finger is introduced into the anal canal and the prostate is palpated for its size, consistency and tenderness. Prostatic massage is contraindicated if there is acute tenderness. Bring the finger first to the right lateral lobe and press it from above downwards. Then repeat the same procedure medially twice. The same is done on the left lateral lobe. This brings the prostatic secretions into the urethra. Then bring the finger in the midline and press downwards. This will express the discharge from the prostatic urethra to the penile urethra. Examine the nature of the secretion and do a gram stain. Clumps of pus cells indicate prostatitis.

INVESTIGATIONS

Urethral Smear

It should be examined for gonococci by Gram stain. In females, the urethral and cervical smear should be examined. A wet smear in normal saline should be examined for *Trichomonas vaginalis* and *Candida albicans*. If there is no frank urethral discharge the urethra should be milked by applying pressure from the posterior aspect.

Two-Glass Test for Urine

The patient should hold the urine at least for 2 hours, and it is passed into two glasses—the first half in one glass and the rest in the second. If only the first glass is turbid or hazy it indicates anterior urethritis. If both glasses are hazy or turbid it shows that there is involvement of posterior urethra or higher up. Look for any threads which consist of shed epithelium lining Littre's ducts.

In case of ulcers, Gram stain should be done from the discharge or slough.

Dark Field Examination

Clean the ulcer with normal saline, press the ulcer and the serum should be collected on a cover glass. Invert the cover glass on a slide, smear the edges with vaseline. Put oil on the cover slip and also on the condenser and examine under the dark field microscope. Spirochetes and *Trichomonas* can be seen.

Tissue smear: In case of suspected donovanosis, a tissue smear should be taken with a toothed forceps. Forceps, crushed on a slide with another slide and both slides should be fixed and stained with Leishman's stain. The organisms are seen inside the monocytes. The organisms may be coccoid, cocco-

bacillary or with a bipolar staining giving the appearance of a closed safety pin.

In cases of amebic ulcer, a wet saline preparation from the edge of the ulcer may show actively motile amebae. If tuberculosis is suspected, a smear should be examined for *M. tuberculosis* by Ziehl-Neelsen method.

Biopsy of the Ulcer

This helps to differentiate syphilis, chancroid, donovanosis, tuberculosis, malignancy and others.

Serological Tests

Venereal Disease Reference Laboratory Test

Venereal Disease Reference Laboratory (VDRL) test should be done in all STD cases to diagnose syphilis. If the test is negative, it should be repeated after 10 days since the test may be nonreactive in early primary stage. The test should be done in serial dilutions in case of suspected secondary syphilis to exclude a prozone phenomenon. In all other cases the test should be repeated after 3 months. It is a nonspecific test. VDRL becomes negative after treatment.

Specific Tests for Syphilis

Specific tests are done to differentiate from a false positive reaction and to know whether the patient had a previous treponemal infection. ***Treponema pallidum* immobilization test (TPI),** fluorescent treponemal antibody absorption test (FTA-ABS) and ***Treponema pallidum* hemagglutination test (TPHA)** are the specific tests used. Of these three specific tests, TPI is very specific, FTA-ABS is very sensitive, but the commonly performed and available test is TPHA. In biological false positive VDRL test, TPHA test will be negative. TPHA usually remains positive life long, even after full treatment.

FTA-ABS IgM test is indicated in case of congenital syphilis to differentiate between infection in the baby and the transmission of maternal reagenic antibodies without actual infection. Presence of FTA-ABS IgM antibodies suggests that the baby is infected.

Cerebrospinal Fluid (CSF) Examination

The cell count, proteins and VDRL should be done to exclude neurosyphilis. In neurological involvent in AIDS the CSF may show diagnostic abnormalities.

Human Immunodeficiency Virus Infection and Skin

Human immunodeficiency virus (HIV) pandemic is continuing for nearly 30 years. Heterosexual contact is the main mode of transmission. Certain skin disorders are highly associated with HIV infection. Serotesting is indicated in acute retroviral syndrome, oral hairy leukoplakia, eosinophilic folliculitis, Kaposi's sarcoma, bacillary angiomatosis, proximal subungual onychomycosis and occurrence of any STD. Viral infections like herpes zoster and molluscum contagiosum, fungal infection like candidiasis, recurrent aphthae and seborrheic dermatitis are common associations.

In the early course of HIV, most dermatological manifestations are typical and respond to treatment. With progressive immunodeficiency, atypical presentations occur. They are usually extensive, recurrent and resistant to treatment.

ELISA Test for Human Immunodeficiency Virus I + II Antibodies

ELISA for HIV should be done in all STD patients, those with multiple partners, homosexuals and those with high-risk behavior. If positive, it should be confirmed by Western blot test.

SECTION

16

Psychiatry

CHAPTER

44 General Considerations

N Krishnankutty

Psychosis, Neurosis, Mental functions, List of signs and symptoms of mental disorders, Classification of mental disorders, Organic and functional mental disorders

INTRODUCTION

The mind is viewed as an organ of the brain. Its existence is inferred from its functions—the mental functions (Table 44.1). These functions are interrelated. Such relationship is maintained even when they become abnormal. For example, when mood becomes abnormal the thinking is disturbed. Memory fails when attention is abnormal. Disorientation occurs as the consciousness is impaired and the like. The abnormalities in the mental functions manifest as the symptoms and signs of mental disorders (Table 44.2). These are highly subjective. Since the signs cannot be clearly separated from symptoms in psychiatry, they are described together, unlike as in physical illnesses. Groups of signs and symptoms are found to occur together and with a particular course and outcome. This phenomenon formed the basis of classification of mental disorders into diagnostic categories (Table 44.3), without reference to specific etiology. For the same reason, the term 'disorder' is preferred in place of illness. Two terms, psychoses and neuroses have traditionally been used in psychiatry.

The term ***psychosis refers*** to a severe form of mental disorder where there is gross disorganization of personality and severe impairment in social functions. These patients fail to realize what is real and what is not. Reasoning, judgment and insight are lost. Hallucinations and delusions may occur schizophrenia, delirum, dementia, mania, and depression are examples of phycosis.

Neurosis on the other hand, is a less severe form of mental disorder with minor impairment in social and personality function. Sense of reality, reasoning and insight are retained. Hallucinations and delusions are absent. Generalized anxiety disorders, conversion and dissociative disorders, obsessive compulsive disorders, and phobic disorders are examples of neurosis. The terms 'organic' vs 'functional' is a dichotomy still alive in psychiatric vocabulary.

MENTAL FUNCTIONS

Mental functions are described in Table 44.1.

Table 44.1: Mental functions

Mental functions
• Mood/affect
• Thought
• Psychomotor activity
• Perception
• Cognition
– Consciousness
– Orientation
– Attention and concentration
– Memory
– Intelligence
• Reasoning and judgment
• Insight

SIGNS AND SYMPTOMS

Signs and symptoms of mental disorders are described in Table 44.2.

Table 44.2: Signs and symptoms of mental disorders

- Abnormal psychomotor activity

Acceleration	Retardation	Perseveration
Agitation	Stupor	Catatonia
Restlessness	Stereotypy	Waxy flexibility
Excitement	Echopraxia	Negativism
Retardation	Perseveration	Posturing

- Abnormal mood

Apathy	Euphoria	Anxiety
Incongruous mood	Exaltation	Irritability
Blunted affect	Ecstasy	LaBella indifference
Elevation	Depression	

- Abnormal thoughts

Formal thought disorders
Loosening of association, flight of ideas, neologism, perseveration.
Abnormal streams
Pressure of thought, poverty of thought, thought block, tangentiality, circumstantiality
Abnormal contents

Delusions	*Types of delusions*	
Suicidal ideas	Persecutory reference	
Obsessions	Grandiose	Poverty
Phobias	Nihilistic	Somatic
	Primary	Secondary

Thought insertion
Though withdrawal
Thought broadcast

- Abnormality of perception

Hallucinations	*Types of hallucinations*
Illusions	Auditory, visual, olfactory, haptic (tactile) and gustatory (pertaining to taste and flavor of food)

Depersonalization
Derealization
Micropsia
Macropsia

- Abnormal consciousness
 Clouding, confusion, stupor
- Abnormal orientation
 Disorientation in time, place and person

Contd...

Contd...

- Abnormal memory
 Amnesia – immediate, recent. and remote; anterograde, retrograde confabulation
- Abnormal intelligence
 Dementia, mental retardation
 Abnormal Judgment – impairment

Table 44.3: Classification of mental disorders

- **Organic mental disorders**
 Delirium, dementia
- **Mental disorders due to**
 psychoactive substance use, e.g. alcohol, tobacco, cannabis opiods
- **Schizophrenia**
- **Mood disorders:** Manic episode, depressive episode
- **Neurotic and stress related mental disorders**
 Generalized anxiety disorders
 Panic disorder
 Phobic anxiety disorders
 Obsessive – compulsive disorder
 Dissociative (conversion) disorders
 Somatoform disorders
- **Sexual dysfunctions** – impotence
- **Personality disorders**
- **Psycological developmental disorders**
- **Childhood emotional disorders**
 Attention deficit
 hyperactivity disorders (ADHD)
 Conduct disorders
 Mental retardation

ORGANIC AND FUNCTIONAL MENTAL DISORDERS

Since early days mental disorders were divided into organic and functional groups. It is called organic when the disorder results from demonstrable physical pathology, e.g. syndrome of dementias and delirium. When no such physical pathological changes are found it is called functional mental disorders, e.g. schizophrenia, mania, depression, and anxiety disorders. At Present, this dichotomy has been found to be not always true. All mental disorders have some type of pathological basis which may be physical, biochemical, genetic or others.

CHAPTER

45 Clinical Aspects of Mental Disorders

N Krishnankutty

Examination of psychiatric patient, Mental status examination, Examination of psychomotor activity, Brief clinical features of common mental disorders

EXAMINATION OF A PSYCHIATRIC PATIENT

The clinical approach in psychiatry begins with examination of the case. Examination of a psychiatric case is similar to that of any medical case. History is taken initially (longitudinal study). It is followed by mental status examination (cross sectional study). It is followed by relevant investigation to arrive at a proper diagnosis. The history is most important. It has to be systematically and very elaborately taken to assess the various levels of mental functioning. The data can be collected by interviewing the patient. An informant to whom the patient is closely known is the best source of information especially in the case of psychosis and mental retardation. It is important to establish a good rapport with the patient in the beginning itself. Make a full record of the data. The scheme is given below.

A. History
1. Identification data
2. Presenting complaints
3. History of present illness
4. History of past illness
5. Family history
6. Socioeconomic status
7. Personal history
8. Premorbid personality

B. Mental Status Examination
1. General appearance and behavior
2. Psychomotor activity
3. Mood (Affect)
4. Thought
5. Perception
6. Cognition
 a. Level of consciousness
 b. Orientation
 c. Attention and concentration
 d. Memory
 e. Intelligence
7. Reasoning and judgment
8. Insight

C. Physical Examination
1. General
2. Systemic

D. Provisional Diagnosis

E. Investigations
1. Biological
2. Psychological

F. Final Diagnosis

HISTORY

Identification Data

The name, age, sex marital status and address are to be recorded for communication and future reference.

Presenting Complaints

A patient with mental disorders may come with varied symptoms. The common ones are violent and aggressive behavior, disturbance in talk and communication, disturbance in sleep, disturbance in appetite, fearfulness, sadness, withdrawal from duties, lack of appetite, sexual function disturbances, suicidal tendencies and self-harm, bodyaches and pains, convulsions, paralysis, loss of consciousness, loss of memory, poor intelligence, and habituation to alcohol and other intoxicants.

History of Present Illness

Derive in detail all about the illness from the very beginning till date. Note the following:

1. How was the onset; acute or insidious?
2. Was there any precipitating or aggravating factors and daily fluctuation?
3. What were the treatment received and what was the result?
4. What was the level of cooperation of the patient?

Leading questions are asked to bring out suicidal tendencies, sexual dysfunctions, delusions, hallucinations and habituation to intoxicating drugs including alcohol.

History of Past Illness

Past physical ills and past mental disorders: The patient may have physical illness and mental disorders previously. Both are important. If a psychiatric disorder was present previously, its nature, course and previous outcome are to be obtained. The present illness may be either an exacerbation or another episode of the previous disorder.

Previous physical illness may bear relation to the present mental disorder. Epilespy and head injury may have psychiatric sequlae. Treatment with steroids can produce mood disorder. Cushing's disease, thyroid dysfunction and Huntington's chorea have their psychiatric counterparts. Encephalitis in childhood can cause mental retardation.

Family History

All details of the family members, their inter-relationship, the family structure, the attitude of other family members towards the patient and the occurrence of psychiatric illness, alcoholism, suicide, and mental retardation in the family have to be elicited. Drawing a family tree is useful for recording.

Socioeconomic Status

Socioeconomic conditions of the patient and the social support he is likely to get are to be enquired into. His source of income and accessibility to treatment and affordability to costly drugs is also important.

Personal History

Get a biographic scheme of the person. Prenatal and postnatal history, trauma and illness during childhood, milestones of development, peer group relationships, physical torture, sexual abuse, educational performance and attainment, occupation, work record, religious beliefs, addiction to drugs, smoking, marital adjustment and details of children are all important.

Premorbid Personality

It refers to the actual personality of the individual before the onset of the illness (morbidity) as change of personality is likely to occur due to the illness. The *'personality'* includes the habitual attitudes and behavior pattern characteristic to an individual (character traits). Find out the general behavior pattern, attitude to self and others, social relations, moral and religious attitude, usual mood and activity, hobbies, likes and dislikes and the response to stress.

MENTAL STATUS EXAMINATION

The examination starts as soon as the patient enters the consultation room and goes hand-in-hand with history taking. Some cases may require more than one sittings for the completion. It is done according to the scheme.

General Appearance and Behavior

The description should be as complete, accurate and life-like as possible. Look at the way of dressing, cleanliness in general, self-care, hair dressing, and behavior towards others.

Note:

1. Is he in touch with the surroundings?
2. Is he restless or slow?
3. Is the patient violent and aggressive?.
4. Are there abnormal responses to external events?
5. Is he cooperative?
6. Is he communicative?
7. Does the patient's behavior suggest that he is disoriented?

Note the presence of any catatonic phenomena, tics, mannerisms or hallucinatory postures.

EXAMINATION OF PSYCHOMOTOR ACTIVITY

It is the mental activity manifested in his physical activity. It is not the same as neurological motor function. Observe the speed or rate of talk, writing or any other activity. The rate may be abnormally low or high. When the rate is high, it is called

increased psychomotor activity (PMA). It is called *acceleration* when it is one of the useful functions, and *agitation* when it is of purposeless and aimless one. If the PMA is slowed, it is called *psychomotor retardation*. It may be so lowered that the patient may become mute and immobile, called *stupor*. Abnormal repetitive activities such as stereotypy echopraxia, echolalia, perseveration and catatonia may be present. The patient may be seen doing same activity again and again continuously without any purpose *(stereotypy of action)*. Similarly the same word or phrase will be repeated *(stereotypy of speech)*.

Some patients may be seen involuntarily imitating the action just seen by him *(echopraxia)* or the words or phrase just heard *(echolalia)*. The patient may give an answer to a question. When a second question is asked following it, at the same time, the answer given to the first one may be automatically repeated few times *(perseveration of speech)* Similarly repetition may occur in carrying out an activity *(perseveration of action)*.

Catatonia refers to the widespread muscular rigidity expressed as waxy flexibility, posturing, negativism, excitement or stupor. Ask the patient to do some deed. He may automatically resist it or may do the opposite of expected one *(negativism)*. The limb of the patient may show wax like rigidity so that it can be placed in any awkward posture for any length of time. *(Waxy flexibility/catalepsy/ flexibilitas cerea)*. *Posturing* is the maintenance of bizarre, fixed, strange, rigid body position for prolonged periods. *Violent* and aggressive activity may be found in excitement.

Clinical Importance of Psychomotor Activity

Mild increase in PMA is called *restlessness* which is found in generalized anxiety disorders and early delirium. Psychomotor activity (PMA) is very high in manic excitement, schizophrenic excitement, alcoholic intoxication, delirium, panic attacks and agitated depression, attention deficit hyperactivity disorder. Echolalia stereotypy, echopraxia, negativism, waxy flexibility are more common in schizophrenia than in organic disorders. Perseveration is more common to organic disorders. The PMA is retarded in depressive illness. Stupor may be found in depressive disorder, catatonic schizophrenia, organic (physical) disorders and dissociative disorders.

Examination of Mood

Affect and mood are two terms used to represent the emotional state. Affect is the momentary feeling tone that accompanies an idea, that what is spoken out. *Mood* is a well sustained emotional state. In clinical practice both may be used interchangeably. Normal mood is *euthymic*; it is neither sad nor elated and it is congruous with the ideas and actions.

Mood may change to abnormal states. Such changes are incongruity, apathy, blunting, elevation, depression, anxiety, irritability and the like. It can be revealed by examining the quality and intensity of mood and its relations to the ideas. Mood has to be assessed subjectively and objectively. Ask the patient how do you feel? How is your mood? The answer to this gives the subjective mood state. The examiner may observe the mood at the same time—the objective mood. Both objective and subjective moods should be the same—*congruous* or *appropriate* mood. If both are contradictory, it is inappropriate or *incongruous*. It is also *incongruous* if the mood and ideas are not in harmony. For example, the patients may be telling his sad news, but he may appear happy. The face may appear mask like with no emotional response to anything (*apathy*).

Examine the degree of intensity of mood. An obvious reduction in the intensity may be seen (*flattened/blunted affect)*. The patient may appear persistently happy and overjoyous for no obvious reason *elevation* of *mood*. When the mood is elevated, find whether it is euphoria, elation, exaltation or ecstasy. *Euphoria* is a mild degree of elevation with exaggerated physical and psychological well being. *Elation* is moderate degree of cheerfulness with increased self-confidence and grandiose ideas. *Exaltation* is severe degree of elation with grandiose delusion. *Ecstasy* is the highest degree of happiness, a feeling of rapture where one may forget oneself. Usually it is short lived. The mood may be lowered or *depressed* as seen by the feeling of sadness, the facial muscles are devoid of tone and become loose, the angle of month sags down, the eyelids tend to fall down. A fearful facial expression appears in *anxiety* mood; where the eyes are widely open, pupils dilated, the facial muscles are tight with prominent grooves. Some patients may show excessive reaction in unpleasant manner to external

stimuli *(irritability)*. The patient may not show any type of emotional concern towards the disability which he is suffering *(La-Belle indifference*).

Examination of thought/thinking: The thought is manifested as talk, writing and gestures. *Normal thought* is relevant to the context and coherent. It follows a logical sequence pattern and grammatical alliance. To find the abnormalities in thought, examine how the thought (talk) is formed, how is the flow (stream), what abnormal contents are there, and if there is any denial of ownership (possession).

Loosening of association, flight of ideas, neologism and perseveration are formal thought disorders. In *loosening of association* the logical sequence pattern is lost and so the thoughts become meaningless and ununderstandable. The grammatical alliances are not held properly. *In-flight of ideas* there is rush of thought and the thought jumps rapidly from one topic to another. They are related to one another and the meaning can be gathered. The patient may use new words not found in the dictionary *(neologism)*. The patient may continually repeat the same answer given to a previous question, without responding to further fresh questions *(perseveration)*.

Examine the stream of the talk. Too many ideas may be rapidly rushed out of the mind *(pressure of thought)*. On the other hand the talk may be scanty and the flow is slow *(poverty of thought)*. The stream of talk may stop abruptly by itself and fails to proceed further, however they may try *(thought block)*. The talk may deviate away from the matter discussed and fails to reach a final goal *(tangential thinking)*. But in circumstantiality after lengthy narration the original goal is reached finally.

Look for abnormal contents such as delusions suicide ideas, obsessions, phobias and other. *Delusion* is an abnormal belief which cannot be shared by others. The notion is false, fixed and cannot be corrected by arguments and evidence to the contrary. It is culturally unacceptable. Usually delusion is reported by the informant of the patient. Some may have *persecutory delusion* that the food given is being poisoned; secret plot is being made to kill him or to take away his wealth; he is spied upon and so on. A news in the media, a gesture observed, a conversation heard, a spitting out seen may be construed as referring to him only and done deliberately by his enemies. *(delusion of reference)*.

The patient may have the delusion that he is very powerful, can do anything for others and has close company with persons of high positions—scholars, scientists, ministers, film stars and the like (*grandiose delusion)*. *Paranoid* delusion is a common term in use. It includes both persecutory and grandiose delusions. A patient in depression may have the delusion that they lost everything and has become too poor *(delusion of poverty)*. In delusions of guilt, the patient accuses himself as a sinner, having done many sinful deeds in the past and wishes to get punishments. Depressives often say that part of their body or the whole body or the world itself is not existing *(nihilistic* delusion). *Delusion of infidelity* is found among couples where the opposite partner is accused of extramarital sexual relation. Some patients may come with delusion that they suffer from serious physical disease (*somatic/ hypochondriacal delusion*) The delusion may be that their mood, thought and actions are controlled by other people outside, (*delusion of control/ passivity/influence*).

Delusion may appear suddenly out of the blue, not preceded by, any other psychological events *(primary delusion)*. Delusion may occur secondary to some other psychological events such as mood change or hallucination *(secondary delusion)*. Thought insertion, thought withdrawal and thought broadcasts are other kind of delusions. *Thought insertion* is the experience that thoughts are not his own but placed in the mind by persons outside. *Thought withdrawal* is the experience that his thoughts are taken way or stolen from his mind as the thought disappears as soon as it comes to the mind. *Thought broadcast* is the experience that others are participating in his thinking so that unspoken thought are known to other persons.

Ideas of *suicide* are not generally expressed they have to be tactfully elicited. Enquire about the life in general and its importance. Ask about the present state of life of the person and his desire to live long. Further it can be asked whether he had wished death at any time. In positive cases enquire about the plans made and of the desuading factors.

Obsessive ideas may be there as part of symptom of OCD, schizophrenia, depression or brain disease. Phobia is a symptom of phobic anxiety disorders.

Examination of Perception

We perceive through the sense organs such as eye, ear, nose, taste buds, and the skin. Thus, the perceptions are visual, auditory, olfactory, gustatory and haptic/tactile respectively. Abnormalities of perceptions such as hallucinations, illusions, macropsia, micropsia and dereality experience may be found in mental and neurological disorders.

Hallucination refers to the vivid sensory experience in the absence of the real object or stimuli around. Thus, there could be visual, auditory, olfactory, gustatory and tactile/haptic hallucinations.

Auditory hallucination (hearing voices/noises). Certain clues for hallucinations may be there. The patient may be seen talking to self, whispering, making gestures, picking something up from clothes and blocking the nostrils with finger tips and the like. Auditory hallucinatory voices may be revealed as complaints that the patient is accused, blamed, talked of obscenely, threatened to be killed, prompted to end life and made fun of. Further they may be seen reacting to it by retorting in the same coin, start quarrelling and even petition to police. When voices are there ascertain the contents of the hallucination and the type of person—*I, II, or III*. Hearing one's own thought spoken aloud are of first person type. Voices arguing or addressing as "you" and yours are of second persons and voices of running commentary, making statements or conversations about the patient are of third person type. Instead of voices there may be noises of any kind in many cases.

Case Reports

A mother sleeping with her schizophrenic daughter was woken up at night hearing the loud laughter of the patient. The patient said the reason; "Cannot you hear? They are calling me. Come, come out. We are here outside. "The mother said angrily." Your madness has come again."

Visual Hallucinations

It is common in delirious patients. They may be startled with complaints that worms, spiders, snakes, millipedes and such insects are crawling over the body. They may try to pick them out. Visual hallucinations may be there in migraine and in LSD and cannabis intoxication.

Gustatory Hallucinations

Depressive patient may make complaint of getting bitter taste without bitter substance. Similar experience may be found in temporal lobe epilepsy (TLE)—gustatory hallucination.

Olfactory Hallucinations

The patient may have olfactory hallucinatory experience of pleasant or unpleasant smell. Get the kind of smell and know whether it is coming from outside the body or emanating from inside.

A case report: A teenaged girl discontinued her studies, withdrew from social activities and resisted marriage till late thirties, all because of her hallucinatory experience that she passed down foul smelling gas frequently. She refused medical help telling that it is true.

Tactile Hallucination

Some patients may have complaints that bugs or insects are crawling under the skin. To some, X-rays, electormagnetic waves or cosmic rays and vibrations falling on their skin may be experienced. But the examiner will not find any evidence. This is the nature of tactile/haptic hallucinations.

Clinical Importance of Hallucination

Hallucinations are pathological, but not always. Hearing divine voices in the air once in a while is a culturally accepted premonition. Visual hallucinations and rarely auditory hallucination occurring as one falls asleep (*hypanagogic* hallucination) and wakes up from sleep (hypnopompic hallucination) are not abnormal. Second and third person auditory hallucinations and hearing one's own thought spoken aloud are suggestive of schizophrenia. Auditory hallucination of derogatory contents favors depressive disorder. Olfactory hallucination of burnt materials are characteristic of temporal lobe epilepsy. Hallucination of bad odor entering the body is experienced in schizophrenia where as passing out foul gas from the body is experienced in depressive disorders.

Tactile/haptic hallucination of worms, creeping under the skin is a feature in cocaine psychosis. Tactile hallucination of X-rays, electromagnetic

waves, cosmic rays falling on the skin is symptom of schizophrenia. Gustatory hallucination occurs in temporal lobe epilepsy (TLE) and depression.

Illusion

It is the phenomenon of misinterpretation of sensory experience under certain circumstances. A rope may be mistaken for a snake and a tree for a ghost.

De-reality Feeling (De-away)

Some patients may come with an experience to their body as if the body or part of the body is not real and changed some way—*depersonalization*. In a similar way the patient may have the feeling as if the surroundings are not real and has changed in some way— derealization.

Clinical importance: Both depersonalization and derealization are found in cases of anxiety disorder, depressive disorder, epilepsy, organic brain disorders and schizophrenia.

Micropsia

The object appears much reduced in size.

Macropsia

The object appears much magnified.

Both micropsia and macropsia are found in TLE and schizophrenia.

Examination of Level of Consciousness

These affect the clarity of the sensorium. The disorder of consciousness includes clouding, confusion, stupor and coma. Functional psychiatric symptoms develop in a clear conscious setting. On the other hand if the symptoms are found to supervene on an impaired state of consciousness, an organic illness has to be considered. In hysterical fainting there is no real loss of consciousness, and they will be aware of the surroundings. The level of consciousness has to be carefully assessed by inspection and interrogation.

Examination of Orientation

Orientation is the appreciations of one's own temporal, personal, and spatial relations at a given moment. *Disorientation* is the disturbance of orientation. Disorientation may pertain to time, place or persons. It may occur in delirium.

Test the Orientation

Ask the patient to give the time of the day without looking into the wrist watch and also the day of the weekmonth and year. Wrong answers convey *disorientation* in time. Ask the patient to name the place where he is now, the name of his locality and the place where the hospital is situated. Errors points out *disorientation in place*. Find whether the patient can identify persons previously known or persons in traditional uniform such as policeman, nurse or doctor. *Disorientation to person* is indicated by the mistakes committed.

Tests for Attention and Concentration

These terms indicate the ability to focus to a particular stimulus and to sustain it. Attention can be assessed during interrogation. Normally, attention is prompt and sustained as long as the stimulus continues. Test whether the attention is normal or abnormal. Attention and concentration can be tested by:

Forward and Backward Counting Test

The patient is made to count 1 to 20 forwards and then backwards. Errors occur when attention is impaired.

Serial Deduction Test

To deduct serially 3s from 40 or 9s from 100. The rate of performance and the errors committed will give an idea of the state of attention and concentration. These factors also depend to great deal on the level of his education.

Digit Span Test

The patient is seated in front of the examiner. In the digit forward test the patient is asked to repeat digits given by the interviewer containing three, four, five, six, seven or eight digits (e.g. 729, 3194, 27106). In the backward digit test, the digit given by the examiner have to be repeated in the reverse order (i.e. 8139 as 9318). 7 digits forward and 5 digits backward constitute normal ability. It is lowered when the attention or immediate memory is impaired.

Impaired attention is called *distractibility*. *Fluctuating attention* is found in delirium. Lack of concentration occurs in generalized anxiety disorders, depressive disorder, schizophrenia, dementia and delirium.

Examination of Memory

Memory includes not only recollection of past events and information but also the process of their registration, retention and storage. Classically three functional levels of memory are followed—immediate, recent and remote. Each has to be assessed separately.

Immediate Memory

It involves the process of registration and retention of information for ultrashort period. It can be assessed by digit span and object test.

Digit Span: (Ref: Test of Attention)

Object Test: The examiner takes five common objects. Show them to the patient. Hide them in five different places. Make the patient understand the objects and the places hidden. Ask some unrelated things to distract the attention. After 5 minutes ask the patient the objects and the places where they are hidden. Incorrect answers indicates impairment in immediate memory.

Recent Memory/Short-term Memory

It subserves the function of retention for short period and the ability to acquire new knowledge. Ask the patient what items of food he had for the previous lunch, persons who has visited him the previous day and what important news were there recently in the press or in the TV. Many such recent information can be checked. Errors indicates amnesia for recent events. The truth has to be verified by the bystanders.

Remote Memory

This term refers to the recollection of events of the long past. Ask the patient to give his date of birth, the name of school where he has studied, date of marriage, the name of the siblings. Mistakes are suggestive of loss of remote memory. It has to be corroborated by relatives. Loss of remote memory is a late event in the disease process.

Clinical Importance of Memory

Loss of memory is called amnesia. Amnesia occurs in many CNS diseases and psychiatric disorders. Easy forgetfulness is a problem among school children. Basically, it is due to poor attention causing failure of registration. Anxiety disorders can also produce apparent amnesia. Amensia and intellectual defect are presenting symptoms in some depressive disorders (pseudodementia). Chronic schizophrenic patients are shown to be defective in memory. Amnesia for selected events is common to hysterical dissociated states (hysterical amnesia). Amnesia may be feigned by criminals to escape punishment. Progressive memory loss is the prominent symptom in dementia. It starts with amnesia for recent events. Amnesia for remote events occurs in the late stages. In head injury a period of amnesia is recorded prior to the state of unconsciousness (*retrograde amnesia*). And period of an amnesia is recorded from the unconsciousness state to the time of regaining continuous memory (anterograde amnesia). It also occurs in epileptic attacks. In case of memory loss, the amnestic gap may be covered by irrelevant and unrelated matters (confabulation). It is a symptom of Korsakoff's psychosis.

Examination of Intelligence

Intelligence is the global capacity of an individual to think rationally, to act swiftly and to adjust adequately to the surroundings. Intelligence can be assessed clinically by knowing his adaptive skills, general knowledge, occupational adjustments, educational achievement, motor skills, management of finance, household and others. It can also be assessed during the interview. Intelligence can objectively be measured by scales of intelligence. Intelligence is expressed as *intelligence quotient*—IQ and the normal is 100 + or – 16 – a whole number. See whether the intelligence is average or subaverage or whether it is subnormal due to brain pathology in dementia. Subaverage intelligence, due to failure in development is called *mental retardation*. Milestones of development will be delayed in such cases.

Examination of Judgment and Reasoning

Judgment is the ability to make right decisions in specific situations. See whether the judgment is normal or impaired. To test judgment certain hypothetical situations are selected. Examples: "What will you do when you see a house on fire? What will you do when you get a wound on your finger? What will you do if you find a stamped, addressed envelop on the road"? Subaverage answers suggest impairment in judgment.

Examination of Insight

Insight refers to awareness of one's own physical and mental health. Ask the patient whether he suffers from any illness or he needs any treatment? The usual answers will be : "I am not sick, I don't want treatment. I have some physical illness and no mental diseases and want treatment. I have some mental trouble and would like to see a specialist". These answers give some ideas on the presence of insight.

Physical Examination

Mental symptoms could occur as manifestations of an underlying physical illness. Similarly, the appearance of physical symptoms could be due to a mental disorder. So a proper and complete physical examination is necessary in every case. Moreover, certain psychotropic drugs cause changes in physical parameters such as pulse rate, blood pressure, body weight, blood counts, kidney, liver functions and ECG.

Provisional Diagnosis

Diagnosis based upon the derived clinical findings could be made at the end of case examination. Relevant investigations help to confirm the diagnosis.

BRIEF CLINICAL FEATURES OF COMMON MENTAL DISORDERS

Delirium

Acute in onset. Sleep disturbance, or reversal of sleep rhythm (wakeful at night and sleeping during day time), confusion, disorientation, excitement, highly anxious or perplexed. Poor attention (distractability). Hallucination especially visual and tactile are more common. Features of the causative physical illness.

Dementia

Often insidious in onset and chronic in course. Impaired memory. Recent memory is lost first and remote memory later. Deterioration of intelligence. Performance intelligence is lost first and verbal intelligence later. Neglect of selfcare. Disinhibited behavior, decline in social and ethical standards. Loose, disconnected talk, with poor content and in coherence. Affective change—elation, depression, irritability.

Schizophrenia

This disorder is chiefly manifested by characteristic disturbances in thinking, perception, mood and psychomotor activity. Formal thought disturbances like loosening of association, neologism, incoherence, echolalia, thought block and tangentiality are characteristic. Delusions are prominent. The most common are the persecutory delusion. Grandiose, religious and somatic delusions are also found. Thought insertion, thought withdrawal and thought broadcasting are common.

Auditory hallucination is the commonest disorder of perception. Commentaries and conversation about the patient and hearing one's own thought spoken aloud are common in schizophrenics. The hallucinatory voices may be threatening, obscene, or accusatory. Haptic hallucinations of X-rays, cosmic rays, vibrations and electromagnetic waves falling on the skin are common.

The mood may be incongruous or blunted or apathetic. In acute cases intense fear is experienced. Psychomotor disturbances are many. Catatonic symptoms like waxy flexibility posturing, negativism and stupor or excitement may be observed. Stereotype, perseveration and mannerism are other disturbances. Violent and aggressive activity may be found in excitement.

Mood Disorders

The essential feature is the primary disturbance of mood. A depressed mood results in depressive disorders and an elevated mood in manic disorders. Episodic and recurrent in nature.

Manic Episode

The mood is elevated—euphoria, elation, exaltation or ecstasy. Increased psychomotor activity. Highly energetic and extravagant. Irrevelent talk, pressure of talk, flight of ideas. Jocularity, grandiose, ideas, delusions, insomnia– (early morning to total insomnia) and *hypersexuality are common*. In the severe cases the patient becomes violent, aggressive, destructive with in coherent talk.

Depressive Episode

Depressed, sad, gloomy mood.

Lack of energy and lack of interest.

Social withdrawal.

Retarded psychomotor activity or stupor. Poverty of ideas, guilt feeling, hopelessness and worth lessness. Pessimistic, suicidal ideas, attempts and other self-harming behavior.

Aches and pains and other vague somatic symptoms. Early morning awakening to total insomnia. Loss of appetite, loss of weight and lack of sexual feeling or impotence.

Generalized Anxiety Disorders

Anxiety is very prominent. This leads to symptoms characteristics of autonomous arousal. Mental and physical symptoms affecting all systems are manifest. Different manifestation may occur in different persons.

Mental symptoms: Unpleasant feeling of fear, tension, worries, feeling of impending danger and disaster. Fleeting attention, poor concentration, difficulty in getting into sleep and fretful sleep.

CNS

Dilated pupil, wide open eyes, marked facial grooves, headache and numbness.

CVS

Chest pain, palpitation, tachycardia, high systolic BP.

GIT

Dryness of mouth, anorexia, abdominal distention, gas, constipation, diarrhea, hot flushes at anal orifice.

Respiratory

Tachypnea, breathlessness, chest pain, choking.

Genitourinary

Increased frequency of micturition, hesitancy, failure of erection.

Musculoskeletal

Restlessness, tremors, tight feeling of muscles (tension) and inability to relax, fear to go into public places, crowds, crowded buses, and to travel alone to distant places.

Cutaneous

Increased perspiration, hot flushes, especially at anal orifices.

Panic Anxiety Disorders

Sudden episodic attacks of severe anxiety with feeling of impending doom or disaster or turning mad lasts for a few minutes. Mitral valve prolapse is an important differential diagnosis.

Phobic Anxiety Disorders

Anxiety attacks provoked by certain specific innocuous objects or situations. At other times they are asymptomatic. Symptom ceases when the object or situation is avoided, e.g. mysophobia (fear of contamination), agoraphobia. In agoraphobia, the fear is to go to public places, crowds, crowded buses, traveling alone and to distant places.

Obsessive Compulsive Disorders

The main features are obsessive thoughts and compulsive behavior and the anxiety associated with it. Obsessions are the recurrent intrusion into the mind of unwanted ideas, doubts, impulses or images despite the effort to avoid it and despite knowing that it is absurd. Compulsions (rituals) are repeated activity due to the obsessive thoughts. Voluntary efforts to resist the activity produce mounting anxiety. Examples: That the hand is contaminated by dirt or germs may be an obsession. In order to get rid of it, the hand is repeatedly washed (compulsion). The door may be locked. An obsessive doubt may arise whether it is locked or not. To verify it, checking behavior is carried out repeatedly (compulsion).

Dissociative (Conversion) Disorders

The features are loss or disturbance of function of sudden onset. Psychological stress (unconscious conflict) may be in the background. There are psychic (dissociative) symptoms and physical (conversion) symptoms. The usual psychic symptoms are psychogenic amnesia, fugue, trance, possession state and stupor. The common physical symptoms are motor (paralysis of any type), sensory (anesthesia, hyperesthesia, blindness, deafness) and visceral (vomiting, retention of urine). The symptoms of the disorder may mimic any disease or disorder. No physical pathology may be found. The patient is emotionally unconcerned about the disorder (La Belle indifference) is significant. Patient gets personal benefits out of the disorder (secondary gain).

Dissociative Amnesia (Psychogenic Amnesia)

Sudden onset of forgetfulness for circumscribed or selective events which are traumatizing to the

person. Nonprogressive—no organic lesions can be detected. Complete recovery is the rule.

Dissociative Fugue

The patient may be wandering away to distant places under a new personal identity. Everything about the past is forgotten including the personal identity. Original identity could be regained spontaneously or by hypnosis.

Trance and Possession Disorders

The personality is affected by an alien spirit—either a devil, divine force, or an expired close relative.

Sensory Disturbance

Any kind of sensory loss may occur. In anesthesia, there is loss of sensation is over well defined areas. It is marked by sharp boundaries. Mark the boundary of anesthesia repeatedly by drawing a line with the pointed end of knee hammer from a sensitive area. It also varies with suggestions. The area does not lie within a dermatome. Glove-and-stocking anesthesia is common. Hemianesthesia is another symptom.

Total blindness and deafness are known conversion symptoms. They can be differentiated from genuine disorders.

Total Blindness

Conversion disorder is to be differentiated from organic blindness. Pupillary reflex is present. Let the patient walk around along obstacles. The patient avoids obstacles. In genuine cases the patient may injure himself. Place a tumbler of water close to the edge of the table. Tell about it to the patient and ask him to take it to the examiner. In conversion disorder the patient may take it without dropping it. The cortical evoked potentials are normal in conversion disorder.

Deafness

It is to be differentiated from organic deafness. Onset is sudden. Stand behind the patient. Ask the patient to look forward. Drop down a few coins without the knowledge of the patient. The patient turns the head backwards due to the auditory reflex which excludes organic lesion.

Motor Disturbances

Monoplegia, hemiplegia and quadriplegia are common. They can be clinically differentiated from true paralysis. The patient lies supine. Place the palms of the examiner under the heels of the patient. Ask the patient to raise the paralyzed limb. No movement may be noted. Next, ask the patient to raise the nonparalyzed limb. A downward thrust may be felt over the palm placed under the paralyzed limb (Hovers sign).

Dissociative Convulsion

The patient may present with seizure like movement (Table 45.1).

Dissociative convulsions (pseudoseizures) mimic epilepsy. It should be distinguished from genuine seizures, but both may coexist.

Hand Drop Test

The patient is supine. Passively raise the paralyzed hand straight above the face and allow it fall down. In genuine paralysis the hand ought to fall on the face. But in conversion disorder somehow the face in evaded by the patient.

Aphonia

Absence of voice production. Ask the patient to cough. Coughing exclude paralysis of vocal cords.

Table 45.1: Distinction between genuine seizures and pseudoseizures

Genuine seizures (Grand mal fits)	*Pseudoseizures (Hysterical fits)*
1. Prodromal symptoms and aura are typical and common	Absent
2. Tonic, clonic and relaxation are the movement patterns and these are synchronous	No such typical patterns Movements are asynchronous one limb may flex and another may extend
3. Serious accident or injury when the patient falls down	Minor injuries, no accidents. The patient falls down on leaning with support
4. Bites the tongue	Nil. Cheeks and lips may be bitten
5. Incontinence of urine is common	Rare
6. Fits last for a minute	Variable
7. Confused when awakened	Clear conscious state
8. No awareness of the events around, during the fits	Awareness present
9. Lethargy may last for about 48 to 72 hours	Active and energic after the fits
10. Corneal reflex absent and plantar reflex is upgoing in the post-ictal unconscious phase	Corneal reflex present and plantar is down going
11. Post-ictal rise of prolactin	Nil
12. EEG abnormalities occur usual in inter-ictal period and ictal period	EEG normal

Mild compression with the thumb over trachea may also evoke cough reflex.

Physical Illness Manifesting with Psychiatric Symptoms

Physical illness may coexist not only in organic mental disorders but also in other mental disorders. In addition, many drugs used in therapeutics may induce psychiatric symptoms. Common psychiatric symptoms caused by systemic diseases are given below.

Depressive Symptoms

Carcinoma infections, neurological disorders including dementia, hypothyroidism, Addison's disease, systemic lupus erythematosus, diabetes mellitus, hyponatremia.

Anxiety Symptoms

Hyperthyroidism, pheochromocytoma, hypoglycemia, withdrawal of sedative drugs.

Fatigue Syndrome

Anemia, sleepdisorders, chronic infections like tuberculosis, diabetes mellitus, hypothyroidism, Addison's disease, carcinoma, Cushing's syndrome.

Weakness

Diabetes mellitus, hypothyroidism, malnutrition, anemia, myasthenia, peripheral neuropathy, other neurological disorders.

Episodes of Paroxysmal Disturbed Behavior

Epilepsy, hypoglycemia, pheochromocytoma, porphyria, early dementia, toxic states, or panic disorders.

CHAPTER

46 Investigations in Psychiatry

N Krishnankutty

Biological investigation, Psychological investigation

INVESTIGATIONS IN PSYCHIATRY

In psychiatry, the clinical findings are much more important than investigations. However, investigations help to identify structural lesions and to confirm the diagnosis and also to monitor the drug treatment. The following investigations are done:

1. Biological
2. Psychological.

BIOLOGICAL INVESTIGATIONS

Routine examination of urine hemogram. Blood sugar, liver functions, kidney function, thyroid functions and ECG are to be done.

Special Investigations

Blood Count

Leukocytosis may be one of the side effects of lithium. Leukopenia may be due to toxicity of drugs like clozapine. These have to be monitored periodically in such cases.

Fasting Blood Sugar

Hyperglycemia and diabetes mellitus could result from some of the newer antipsychotic drugs.

Periodic hypoglycemic attacks in insulinoma may cause anxiety episodes.

Liver Functions

Serum bilirubin, SGOT and SGPT may increase in alcoholic liver disease, and also be the result of toxicity to drugs such as carbamazepine, valproic acid and tacrine. Periodic monitoring is required.

Renal Functions

Serum creatinine and blood urea levels may rise as side effects of lithium. These have to be periodically monitored. Other drugs can also produce renal damage which has to be taken care of.

Serum Electrolytes

Hyponatremia may be due to general causes such as fluid and electrolyte loss. In psychiatric practice, drugs like lithium leads to hyponatremia. Hyponatremia may manifest as depressive symptoms, anxiety symptoms and fatigue. These may be mistaken for primary psychiatric disease.

Lactate Test

This is a suggestive test of panic disorders. Intravenous infusion of sodium lactate precipitates the panic. Alprazolam or lorazepam, can be used to alleviate the symptoms.

Narco Test

This test is used to distinguish between catatonic stupor occurring in schizophrenia from those occurring in other organic diseases**.** Schizophrenic stupor improves and organic stupor worsens on IV administration of thiopentone sodium or amytal sodium.

Screening Tests in Urine

When substances abuse is suspected, examination of urine may give the clue of the toxic agent. In acute intermittent porphyria, which may present with psychiatric disturbances presence of porphobilinogen in urine helps to establish the diagnosis.

VDRL Tests

Neurosyphilis, which presents as general paralysis of the insane is characterized by gross psychiatric abnormalities. VDRL test done in blood and CSF is confirmatory.

HIV

In case of extramarital relations and substance abuse or when there is a chance of vertical or accidental exposure. AIDS should be excluded by appropriate tests.

Thyroid Functions: T_3, T_4, TSH

Hypothyroidism may be the cause of depression and dementia. Lithium may produce hypothyroidism. Hyperthyroid patients may present with symptoms of anxiety or agitated depression.

Dexamethasone Suppression Test

In major depression, *the normal response of* suppression of endogenous glucocorticoids in response to externally administered dexamethasone does not occur. False positives tests may develop at times.

Prolactin Level

Increase in the prolactin level may develop as an adverse effect of antipsychotic drugs. This may produce gynecomastia, amenorrhea, and loss of libido.

Prolactin levels may be used to distinguish between genuine seizures and pseudoseizures. Elevation of prolactin levels occurs soon after genuine seizures, not in pseudoseizures.

Body Weight

Increase in body weight is observed in the case of the psychotropic drugs. Hence, regular weight monitoring is indicated. Increase in body weight is a good prognostic sign in the treatment of anorexia nervosa.

X-ray skull can help to diagnose rise in intracranial tension, secondary deposits and intracranial calcifications.

Electroencephalogram

This may help to distinguish metabolic stupor and coma. Electroencephalogram (EEG), taken with sphenoidal electrodes might help to identify complex partial seizures (temporal lobe epilepsy) that can present with episodic behavior abnormalities.

Evoked Potentials

Studies of visual evoked potentials and auditory evoked potentials can help to establish intactness of visual and auditory pathways and to distinguish hysterical blindness or deafness from organic disease.

ECG: Cardiac conduction defect may occur as side effects of lithium, imipramine and other drugs. These have to be monitored.

Computed Tomography

Computed tomography (CT) is very helpful to delineate anatomical lesions in intracranial regions and extracranial structures. CT with contrast, and angiography bring out cerebrovascular lesions, angiomatous malformations and subdural hematomas. Digital subtraction angiography brings out the vascular anatomy more clearly.

Magnetic resonance imaging (MRI) is very useful to study lesions which are not clearly brought out by CT. MRI is more useful to visualize small lesions, lesions in the white matter and those in the posterior fossa. MRI also gives clues about the pathological nature of the lesion.

Positron emission tomography (PET) gives information about the cerebral blood flow and metabolism. Its use in clinical settings is limited, as it is most expensive and is available only in a few centers.

PSYCHOLOGICAL INVESTIGATIONS

Psychological investigations are done under special circumstances in order to help the clinical diagnosis and assess the outcome of treatment.

Commonly used tests can be classified as:

1. Ability tests
2. Personality tests.

Ability Tests

These test the mental ability or potential of a person. These include:

1. Intelligence tests, and
2. Aptitude tests.

The former is used more often in clinical settings.

Intelligence Quotient

Intelligence quotient (IQ) is a concept proposed by psychologist William Stern in 1912. Stern defined it as a constant relationship between chronological age (CA) and mental age (MA). IQ is obtained by dividing the mental age by chronological age and multiplying by 100.

$$IQ = \frac{MA \times 100}{CA}$$

Normal IQ is 90—110

The concept of mental age is introduced by Alfred Binnet in 1905.

Mental age is calculated from the standard intelligence tests. *Wechsler* developed a set of tests for people at various age levels. The tests include:

WISC Wechsler intelligence scale for children aged 5 to 15 years.

WAIS Wechsler adult intelligence scale for persons aged above 15 years.

Bhatia's short scale of intelligence is a modification of Binet-Simon intelligence test and this is widely used in India. The intelligence scales are individual tests with two categories of sub tests—verbal and performance.

Verbal sub-tests reveal the ability to handle language. Performance sub-tests assess the ability to handle motor skills. In early stages of dementia performance intelligence is impaired much more than the verbal intelligence. Performance subtests are more helpful in people with limited verbal skills, foreign backgrounds or poor education, provided they can understand the instructions. Such individuals frequently do better on performance tests than on verbal tests.

Personality Tests

1. Projective tests, and
2. Nonprojective tests.

Projective tests reveal the manner in which a person responds to a vague or ambiguous stimulus and this is often a projection of his underlying mental process and motives.

Common projective tests are *Rorschach Ink Blot test, Thematic Apperception Test, Sentence Completion Test* and *'Draw-A- Person' Test.*

Rorschach Ink blot Test

It is one of the most widely used projective psychological tests. The test kit consists of 10 cards, each one with an ambiguous inkblot. Five are in black and white. The patient is given these cards and asked to give his comments. After the comments, a few clarification questions are asked Card No. 2 would be interpreted by one patient as one pair of bears in a fighting posture, whereas another may visualize it as the lungs of an animal. One may describe more of human features, another one, animal features, still other inanimate objects. Some may visualize movements, others may consider it static. The internal psychological concerns and conflicts of the patient are projected on to the ambiguous inkblots. Hence, the responses reveal the internal psychological world of the individual. It is useful test to assess the personality and psychological conflicts. It also helps in the differential diagnosis of psychiatric disorders when used in conjunction with an informative history and mental state examination.

Thematic Apperception Test

It is a projective test that gives an idea about the interpersonal relationships of an individual and his inner psychological world. The test kit consists of thirty cards, each depicting a social situation—a theme. The individual is asked to tell a story with a beginning, theme and ending, based on the picture in the card. For example, card No. 3 M shows the picture of a man in middle age and a teenager standing by his side. The boy's face is quite grim and the man's face is serious. One patient may interpret this as a father scolding the son for a wrong deed. Another one may think that both the father and son are worried about a common domestic problem. A third interpretation would be that both are plotting a scheme against a hostile neighbor or undesirable relative. In other words, the individual projects his inner psychological conflicts or concerns and interpersonal stresses into the ambiguous social situation depicted in the card and makes a story accordingly. Thematic apperception test (TAT) is useful to understand the dynamics of behavior and in planning psychotherapy.

Sentence Completion Test

It consists of about 100 incomplete sentences. The patient has to complete the sentences the way he likes.

For example:

I often wish ————————

My mother ————————————, etc.

Performance of this test gives an idea of the mental processes of the patient.

'Draw-A-Person' Test

The patient is instructed to draw a picture of a person. The projective hypothesis implies that patients will symbolically project their own personality characteristics on to the drawing. It can be used as a test of intelligence.

Nonprojective Tests

Commonly used tests include:

1. Minnesota multiphasic personality inventory (MMPI): Inventory is a written list of several things. The inventory contains 566 items to be looked into—'true/false items', items of self-report format and primary scales pertaining to personality factors.
2. 16 Personality factor questionnaire (16 PF): It also contains true/false items self-report format and 16 dimensions related to the personality.

Psychiatric Rating Scales

Though the psychiatric signs and symptoms are subjective, they can be measured (rated) by using standard rating scales. The scales are questionnaires, interviews or check lists. The rating is done on a 3 point scales (0,1, 2) or 5 point scales (0,1,2,3,4) or 10 point (0-9). It can be rated on such scales as none, mild moderate and severe. A number of scales are available for assessment.

For example:

- Brief psychiatric rating scales (BPRS)
- Hamilton's rating scales for anxiety (HAM–A)
- Global assessment of functioning (GAF) scale
- Abnormal involuntary movement scale (AIMS).

SECTION

17

Ophthalmology

CHAPTER

47 Ophthalmology: General Considerations

N Vijayalakshmi Ammal, V Sujatha

Anatomy and functions of ocular structures

ANATOMY AND FUNCTIONS OF OCULAR STRUCTURES

Anatomy of the Eye

The eye is lodged in the orbit which is almost pyramidal in shape with the optic foramen at its apex. Posteriorly the bony orbit has three openings—the optic foramen, the superior orbital fissure, and the inferior orbital fissure. The optic nerve and ophthalmic artery pass through the optic foramen. The superior orbital fissure transmits the ophthalmic veins, the third, fourth and sixth cranial nerves which supply ocular muscles and the ophthalmic branch of the trigeminal nerve. The infraorbital nerve and artery pass through the inferior orbital fissure. In addition to the eyeball, the orbit contains extraocular muscles, lacrimal gland, blood vessels, nerves, fat and fascia. The ophthalmic artery and its branches supply ocular structures. Orbital veins empty into the cavernous sinus through ophthalmic veins.

Nerve Supply to Orbital Structures

Third, fourth and sixth cranial nerves supply the external ocular muscles. The third also supplies motor fibers to the sphincter pupillae and ciliary muscles. Dilator pupillae is supplied by sympathetic fibers derived from C8 to T3 spinal segments. Sensory supply to the eyeball and orbit is derived from the ophthalmic and maxillary divisions of the fifth cranial nerve. Ciliary ganglion, which lies to the outer aspect of optic nerve receives motor fibers from third and sensory from fifth cranial nerves and sympathetic fibers from carotid plexus. It gives off short posterior ciliary nerves which enter the posterior part of the eyeball.

The Eyeball

The eyeball is made up of imperfectly elastic tissue consisting of the transparent cornea in front and opaque sclera behind. The cornea is 11 mm in diameter, it is avascular and its sensory supply is by the trigeminal nerve. ***Cornea has the richest sensory nerve supply in the body***. The portion bounded by the two eyelids is the palpebral fissure. The palpebral conjunctiva which is a transparent membrane covers the anterior part of the sclera. The junction of cornea and sclera is the limbus. The angle formed by the bulbar conjunctiva and the tarsal conjunctiva is the fornix. The optic nerve pierces the sclera 2.5 mm internal to the posterior pole. The retina and the uveal tract line the inner aspect of the sclera. The uveal tract consists of the iris and ciliary body anteriorly and the choroid posteriorly. The sphincter pupillae and the dilator pupillae regulate the pupillary aperture.

Ciliary body secretes aqueous humor and the ciliary muscle acts on the ligaments of the lens to control its convexity during accommodation for near vision. The retina consists of seven neural layers formed by three strata of cells and their synapses. The fovea centralis which contains only cones is situated 3 mm to the temporal side of the optic disk and it can be distinctly seen on ophthalmoscopy.

Fovea centralis is the most sensitive part of the retina. It is surrounded by the macula where ganglion cells and plexiform layers are heaped up and nuclear layers are thinned out. The nerve fibers of the retina converge towards the optic disk and form the optic nerve. Fibers of the optic nerve pass backwards through the lamina cribrosa, which is formed by interlacing connective tissue fibers.

The Lens

The lens is biconvex and transparent. It is developed from ectoderm. Central part contains the oldest cells and the periphery, the youngest. Anterior surface is less convex than the posterior. The lens is suspended behind the iris and in front of vitreous by suspensory ligament. The lens is an unique organ in that the cells and proteins once formed, are never turned over. The center of the adult lens contains cells and molecules formed *in utero*. The lens continues to grow throughout life. Newly formed cells elongate and lose their nuclei and organelles and become fibers added to the outermost layers of the cortex. ***Aging is an inevitable process that continues, but under optimum conditions the lens is programmed to remain transparent even up to 120 years. Cataract is the single most frequent cause of blindness.***

Anterior Chamber

It is the space bounded in front by the cornea and behind, by iris and the portion of the anterior surface of the lens exposed at the pupil. It is about 2.5 mm deep in the center. It is filled with aqueous humor. Angle of the anterior chamber is the peripheral recess of the anterior chamber bounded posteriorly by the root of the iris and ciliary body and anteriorly by corneosclera.

Posterior Chamber

It is the triangular space between the back of the iris and anterior surface of the lens.

Eyelids

Eyelids consist of skin, loose connective tissue, muscles, tarsus, fascia and conjunctiva from before to backwards. They contain numerous glands, blood vessels, lymphatics and nerves. The skin is thin and elastic and connected to subjacent muscles by loose areolar tissue. Eyelids are free of fat. Anterior lips of the lids are rounded and eyelashes arise from them. The posterior margins are sharp. The Meibomian glands open in front of the posterior margin. The upper eyelid is elevated by levator palpebrae superioris and both the eyelids are closed by the orbicularis oculi. In addition, the upper eyelid contains Mueller's muscle which maintains a tonic upward pull.

Lymphatics from eyelids drain into preauricular, submaxillary and submandibular nodes. Oculomotor nerve supplies the levator and facial nerve supplies the orbicularis. Sympathetic nerves supply the Mueller's muscle. The lids protect the eyes from injury and excessive light. Blinking of the eye lubricates the eyeball regularly with tears and glandular secretions.

Lacrimal Apparatus

It consists of the lacrimal puncta, canaliculi, sac and the nasolacrimal duct. Excess tears drain into the inferior meatus of the nose.

Extrinsic Muscles of the Eye

Six muscles—4 recti and 2 obliques move the eyeball. Arising from the orbit they are all attached to the sclera. The four recti—superior, inferior, medial and lateral arise from the apex of the orbit. Their anterior attachment to the eyeball is 7.7, 6.5, 5.5. and 6.9 mm respectively behind the corneal margin. The superior oblique arising from the upper and inner margin of the optic foramen, runs forwards, passes through the fibrous pulley and gets attached to the upper and outer portion of sclera behind the equator. The inferior oblique has its origin from the lower and medial wall of the orbit. Like the superior oblique, this is also inserted behind the equator into the outer aspect of sclera.

In the primary position, the axes of the vertical recti make an angle of 25º and those of obliques, 51º with the visual axes. The superior oblique is supplied by the 4th cranial nerve and the lateral rectus by 6th. All the other muscles are supplied by the 3rd cranial nerve. The action of these muscles and testing their function is given along with neurology.

CHAPTER

48 Examination in Diseases of the Eyes

N Vijayalakshmi Ammal, V Sujatha

History, Subjective examination, Visual acuity, Field of vision, Squint, Examination in focal lights, Eyelids, Conjunctiva, Cornea, Anterior chamber, Iris, lens, Ophthalmoscopy, Fundus changes in a systemic diseases, Refractive error, Proptosis

Examination of the eyes forms an integral part of clinical medicine and gives valuable information about diagnosis of not only ocular disease, but also many systemic diseases like meningitis and intracranial tumors. The typical order of examination can be under following headings:

1. History
2. Visual acuity
3. Testing ocular movements
4. Examination of eye is diffuse light
5. Examinations in focal light preferably using slit lamp
6. Fundus examination
7. Special investigations as required by 5 and 6

HISTORY

- Chief complaint of the patient past ocular complaints
- Family history of eye problems
- History of allergy to drugs
- History depending on the presenting complaint can be brief or elaborate. The main complaints pertaining to the eye are:
 - Visual symptoms
 - Pain in the eyes
 - Redness in the eyes
 - Watering
 - Headaches and colored haloes

Visual Symptoms

The most common visual symptom is blurring of vision or loss of vision which could be gradual or sudden in onset. There could be specific visual symptoms like:

- Photophobia—intolerance to light
- Photopsia—flashes of light
- Floaters—seeing spots in front of eyes
- Scotomas—blind areas in the visual field
- Amaurosis fugax—transient blurring of vision
- Hemianopia—seeing only half of the field of vision
- Diplopia double vision.

In the very young, marked fall of vision is due to diseases like:

- Congenital and developmental cataracts
- Congenital glaucomas
- Vitamin A deficiency
- High degree of refractive errors
- Hereditary degenerative retinal disorders
- Infective and inflammatory diseases of the eyes, e.g. congenital toxoplasmosis

In young adolescent and adults common causes for gradual progressive diminution of vision are:

- Refractive errors.
- Corneal opacities
- Inflammatory and infective diseases of the eye
- Retinal degenerative disorders

- Retinopathies especially diabetic retinopathy
- Optic nerve involvement in various diseases especially in demyelinating diseases

Gradual Loss of Vision in the Elderly

Ocular Causes

- Senile cataract
- Glaucoma
- Age related macular degenerations
- Retinopathies, especially diabetic retinopathy

CNS Causes

- Optic atrophy secondary to meningitis.
- Intracranial tumors especially pituitary adenoma
- Demyelinating diseases
- Cortical lesions involving occipital lobe such as injuries, ischemia and tumors

Other ocular causes of blindness include acute congestive glaucoma, opacities in the cornea, lens, or vitreous, injuries to the eye and neurological causes like optic neuritis, optic atrophy and retinal degenerations.

Night blindness is defective vision, often experienced when the level of illumination is low, as occurring at dusk. In India, the most common cause is deficiency of vitamin A. Other less common causes include retinitis pigmentosa, late stages of glaucoma and various types of retinal degenerations.

Alteration in the Perception of Color

Xanthopsia is the phenomenon of seeing objects as yellow. This is a common complication of drug toxicity, especially digoxin.

Indistinct Images and Distortion of Images

Indistinctness of the images is usually caused by refractive errors of the eye such as hypermetropia, myopia or astigmatism. Distortion of the object, its size and shape is caused by macular lesions such as macular edema or macular bums often resulting from watching eclipses directly. Cataract is one of the more common causes of loss of vision above the age of 50 years.

Pain

It may be felt in the eye due to ocular lesions such as glaucoma, iritis, optic neuritis, orbital cellulitis or herpes zoster ophthalmicus. Sometimes pain arising from ocular causes may be referred to other parts of the head as headache.

Lacrimation: Denotes the excessive secretion of tears as is seen in conjunctivitis and keratitis.

Epiphora: It is excessive watering from the eyes due to inefficient drainage of tears through the lacrimal passages.

SUBJECTIVE EXAMINATION

Subjective examination of the eyes consists of tests for:

1. Visual acuity
2. Field of vision
3. Color vision

Visual Acuity

Each eye is tested separately both for near and distant vision. Visual acuity for distance is tested using objects kept 6 meters in front. Snellen's test types are used. Snellen's chart consists of square shaped letters arranged in seven lines. The size of the letters diminish progressively from above downward. Normal subjects can read the upper line at 60 meters and the lowermost at 6 meters distance. Other lines should be read at 36, 24, 18, 12 and 9 meters from above downwards. The subject is made to read the lines first with the right eye and then with the left, the other eye being covered. The line up to which he can see distinctly is recorded. If there are refractive errors, the lenses required to correct the same are also determined by trial and error method. The acuity of vision is expressed as a fraction, the numerator being the distance at which the patient clearly sees the letters and the denominator being the distance at which normal eyes should see clearly. Normal eye can read the smallest row of letters at 6 meters, i.e. the visual acuity is 6/6. If he can see only the top line at 6 meter distance vision is 6/60.

Ordinary test types cannot be used for young children who cannot read. Simple pictures constructed on Snellen's principles may be used. For illiterates 'E' tests may be employed.

Examiner holds letter 'E' of various sizes and patient is asked to identify the direction to which the limbs of the letter point or to hold similar letters in the same position (Fig. 48.1).

If the patient cannot read even the top line, he is brought closer to the chart and the distance at which he can see clearly is measured. If he can read at 3 meters, the vision is 3/60. If he cannot read the

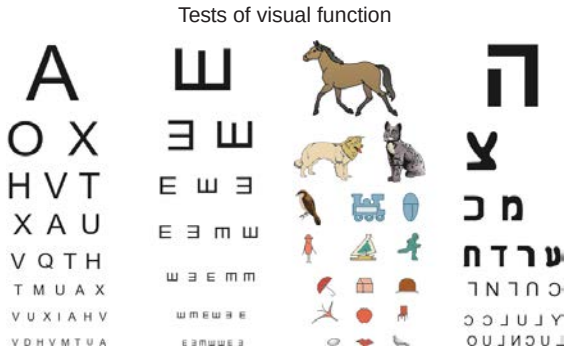


Fig. 48.1: Various types of Snellen's charts to suit literate and illiterate patients and children

letter even at 1 meter, he is asked to count the examiner's fingers held at 30 cm in front. If he can count, the vision is: V = counting finger (CF).

If this is not possible, the examiner's hand is moved in front of the patient's eyes. If he can appreciate this movement V = hand movements (HM). If vision is less than HM, the visual acuity is perception of light (PL). When vision is reduced to PL, the next step is to throw light from different directions. If the patient can indicate the direction of the source of light his vision is expressed as *"PL with projection of light accurate"*.

Pinhole Vision

Pinhole vision is tested when visual acuity is better than 6/60. A pinhole aperture is placed in front of the eye to ascertain any improvement in acuity. A pinhole admits only central rays of light that require refraction by cornea or lenses. Through the pinhole, patient's visual acuity should improve 2 or 3 lines if the cause of diminished vision is refractive error and not in eye diseases like cataract or macular degenerations.

Contrast Sensitivity Test

This is used to test the visual acuity at various special frequencies and contrast levels. The patient is made to identify letters of the same size with diminishing contrast relative to the white background. This test is more sensitive in detecting visual defects caused by lesions of the visual pathway as in optic neuritis

Field of Vision

Field of vision represents the limits of peripheral or indirect vision. It is the area within which an object can be seen while the eye fixes on a spot of light or object. There are several methods of testing the field of vision. A simple but useful bedside method is the confrontation test in which the examiner compares the patient's visual field with his own.

Method

Patient and the examiner sit facing each other at a distance of about 1 m, the eyes being at the same level. Both eyes are tested separately. To test the right eye, the patient keeps his right eye open and the examiner looks with his left eye. The other eye is kept closed. The examiner brings his outstretched left index finger or any test object from periphery inwards, always keeping the object equidistant between the patient and himself. Patient is instructed to indicate as soon as he sees the examiner's fingers or the object. The field is tested in all directions, i.e. lateral to medial, medial to lateral, above downwards and below upwards. After testing the right eye the examiner tests the patient's left eye, this time the examiner's right eye and right hand are used. Normal visual field extends 100° to the temporal side, 55 to 60° nasally, 60° upwards and 70° downwards. Defects in the visual field are called scotomas. Confrontation method can detect gross defects such as constriction of visual field, hemianopia and quadrantanopia and scotomas (Refer Figs 32.2 A to D).

Perimetry

Accurate charting of the visual field is done by perimetry. Perimeter consists of a half sphere within which a spot of light or test object can be moved. A chart which has concentric circles marked upon it is fixed at the back of the perimeter. The patient's head is supported on a chin rest. One eye is covered and the other is fixed upon an object placed at the center of the arc which is about 1/3 meter away. Different test objects which may be white or colored, with diameters of 1, 3 or 5 mm are moved from periphery to center along the radius of the arc up to the point of fixation.

The points at which the object is first seen in the different meridians are recorded upon the chart. Scotomas are recognised by the patient losing sight of the object when moved further. Graphic record of the visual field is made by connecting all these points and the scotomas if any. At least two objects of different sizes and eight meridians must be employed. The fields for different colors are different. The fields for blue and yellow are about

10° less in all directions than that for white. Fields for red and green are smaller by another 10°. While expressing the result of perimetry, size and color of test object, the nature of illumination used and the distance of the eye from the fixation point should be mentioned. For detecting central and paracentral defects within the central 30° radius, i.e. central field, *Bjerrum's screen* is used.

These simple methods of kinetic perimetry have been replaced by static perimetry in modern instruments. For example, in Rubinger perimeter stationary test objects are projected with variable light intensity. *Friedman's visual field analyzer* is a semiautomated perimeter in which the central 25° field is studied at specific points by suprathreshold testing.

Automated perimetry is more popular in ophthalmology and neurology at present. It consists of computerized visual field testing. Static threshold of retinal sensitivity is estimated by presenting randomized stimulus. The field plotted is reproducible and more sensitive. Octopus and Humphery field analyzers are examples of modern computerized static perimeters.

Abnormalities of Visual Fields

See Section 11—Chapter 32 Neurology.

Color Vision

See Section 11—Chapter 32 Neurology.

SQUINT

Squint (strabismus) is the condition in which the visual axes of the right and left eyes do not bear toward an objective point simultaneously. The patient is unable to direct both eyes simultaneously toward a point.

Though gross squint may be detected on inspection, lesser degrees escape attention. An approximate estimate of the degree of squint can be made by noting the corneal reflection, i.e. images of objects held in front of the cornea. Normally, the images falling on the cornea should be symmetrical and at the center of the pupils. In squint the images are seen asymmetrically. If the corneal reflection on the squinting eye is at the edge of pupil, the angle of deviation is 20°, if it is at the edge of the cornea, the angle is approximately 45°. Presence of squint is confirmed and quantitated by the cover test. Three common tests done to identify and measure degree of squint are:

- Bruckner or red reflex test
- Corneal light reflex test
- Cover test

Bruckner Test

A direct ophthalmoscope light is thrown into the patient's eyes and observe for red reflex in both the eyes. The reflex in the strabismus eye will be brighter than the nondeviated eye.

Corneal Reflex Test

The reflexion of light on the cornea is observed in primary gaze. In normally aligned eyes the image should be central and symmetric on both the corneas.

Hirschberg's Test: Patient is asked to look directly at a flash light held ½ m in front of the eye. Asymmetric position of light reflection on cornea indicates deviation. Nasal position of reflection in one eye denotes exodeviation and temporal position of reflection denotes esodeviation. The angle of deviation can be roughly measured by the amount of deviation of reflection from the center of pupil. Each mm deviation equals 7° (degree) or 14 prism dioptres. A light reflection at pupillary border corresponds to 15° degrees, between the limbus and pupillary border 30° degrees and at limbus 45°.

Krimsky's Test: It is same as Hirschberg test, but in this prisms of increasing or decreasing power are held in front of the fixing eye until the corneal reflex in the deviating eye is centered. Strength of final prism gives the amount of squint in prism dioptres.

Cover Test

Method: A spot of light or a fixation object is held 50 cm in front of the eyes and the patient is instructed to focus on it. If one eye is suddenly occluded the other eye does not show any deviation in normal subjects. In the presence of squint the seeing eye will exhibit deviation. This movement is noted. This test is repeated for the other eye also. The direction of movement of the unoccluded eye gives the nature of squint. If the movement is outwards, obviously the eye must have been in a convergent position before occlusion, i.e. convergent squint. If the movement is inwards the eye was in divergent squint.

Primary and Secondary Deviation

In any squint when one eye fixes an object the other eye deviates. In concomitant squint this deviation is equal when either eye fixes. But in paralytic squint, the primary deviation, i.e. the deviation of squinting eye when normal eye fixes is less than the secondary deviation, i.e. the deviation of the sound eye when the paralyzed eye fixes.

Ocular Movements in Six Cardinal Directions of Gaze

- Levoversion—looking to the left
- Dextroversion—looking to the right
- Levo elevation—looking to left and up
- Levodepression—looking to left and down
- Dextroelevation—looking to right and up.
- Dextrodepression—looking to the right and down. Convergence should also should be tested.

Figure 48.2 shows normal movements of the eyeball and Figure 48.3 represents various types of squint.

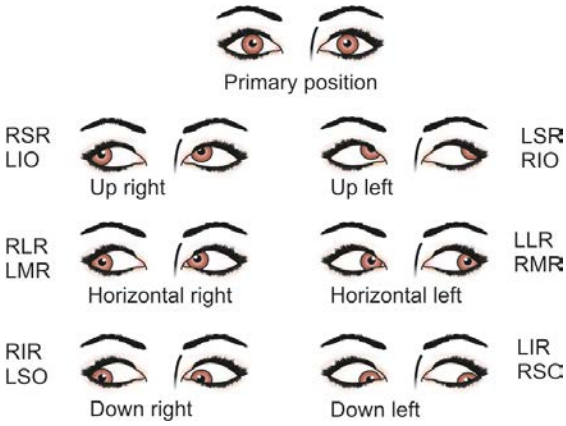


Fig. 48.2: Normal movements of the eyeball. *Note:* RSR, LIO, etc. give the extraocular muscle affected

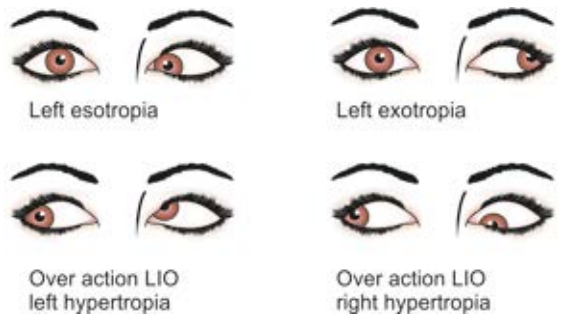


Fig. 48.3: Various types of squint

Head Posture

Normal head posture is erect. Abnormalities like head turn, head tilt, chin elevation or depression are seen in paralytic squint inorder to avoid diplopia.

Facial Asymmetry

Asymmetry could be congenital or acquired. Ophthalmic causes include ptosis, facial palsy, proptosis or tumors involving lids, face, etc.

Interpalpebral Aperture

The part of eyeball exposed between lids is widest in the middle. Inner and outer angles are called canthi. Medical canthus is more or less rounded and lateral angular. Normal upper lid covers 2 mm of normal upper cornea and lower lid just touches the lower limbus. Palpebral fissure is narrow in ptosis and inflammatory conditions of eye and lids and wide in facial palsy and proptosis.

EXAMINATION IN FOCAL LIGHT

This is a very important step of examination of the eyes. Focal light could be a flash light from a torch, condensing lens focusing light from a distant source of light in to the eye. Simple magnifiers like a corneal loupe can give better visualization under magnification. Examination of eyes using slit lamp gives good magnification, illumination and stereopsis (Fig. 48.4).

Slit lamp is a clinical microscope having 2 parts mainly. One giving magnification, illumination and resolution and the other, giving adjustments to alter the angulation, width, and height of the slit lamp beam. Commonly used magnification are 10x, 16x and 25x. Modern slit lamps provide high degree of precision. Several accessories can be used in the instruments. They are:



Fig. 48.4: Slit lamp in use



Fig. 48.5: Left eye shows ptosis



Fig. 48.6: Third nerve paralysis–left with ptosis left. *Note:* Overaction of left frontalis raising the eyebrow

- *Applanation tonometer*—to measure intraocular pressure (IOP)
- *Fundus examination* using various lenses
- Lens—58.6 D: Convex lenses, e.g. 90 D lenses, 78 D lenses.
- *Pachymetry devices*.
- *Gonioscopy lenses*.
- *Photography devices*.
- *Treatment modalities* for delivering laser to intraocular structures.
- *Filters* can be used to observe staining of the anterior segment of the eyes.

The cornea, anterior chamber, iris, pupil and lens can be examined using focal light. Using whatever light type of focal illumination and magnification we start examining each structure in the following order:

- Lids
- Conjunctiva
- Cornea
- Anterior chamber
- Iris
- Pupil
- Lens.

When slit lamp with accessories are available posterior segment can also be evaluated using special lenses. Intraocular pressure can be checked using applanation tonometer and gonioscopy can be done to evaluate the angle.

EYELIDS

Note the following:

1. Normal position and contour of lids.
2. Direction of eyelashes.
3. State of lid margins.
4. Swelling of the lids.
5. Discoloration of lid.
6. Tarsal conjunctiva and its abnormalities.
7. Puncta.

Normal Position and Contour of Lids

Abnormalities we see are:

- Deformities of lid margin
- Entropion—inversion of lid margins.
- Ectropion—evertion of lid margins.
- Coloboma of lid—full thickness of eyelid defect usually congenital.
- Retraction of eyelid usually seen in dysthyroid disorders. Lid lag.

Ptosis is drooping of the upper eyelid (Fig. 48.5). It may be complete or partial. It may be due to mechanical causes like thickening of the upper eyelid or paralysis of levator palpebrae. Mechanical ptosis occurs in trachoma and fibrosis of upper eyelids with thickening of the tarsus. Though the eyelid droops, it can be elevated on voluntary effort. Paralytic ptosis is due to third nerve paralysis and the upper lid cannot be elevated on voluntary effort. Usually it is accompanied by paralysis of the other muscles supplied by the third nerve, especially superior rectus (Figs 48.6 to 48.8).

Ptosis may also occur as a congenital abnormality. Often the eyelids cannot be fully elevated voluntarily. In some cases, the ptosed lid may retract during movements of the jaw such as chewing or opening the mouth. This is called *Marcus Gunn phenomenon.* Corneal aspect of the upper eyelid is examined by everting it. Figure 48.9 shows the method to evert the upper eyelid.



Fig. 48.7: Third nerve palsy left. *Note:* Divergent squint of left eyeball due to unopposed action of left lateral rectus



Fig. 48.9: Method to evert the upper lid



Fig. 48.8: Third nerve palsy left on testing eye movements adduction of left eye is absent



Fig. 48.10: Grade IV senile ectropion left eye. *Note:* Everted punctum (arrow)

Entropion: Lid margin is turned inwards carrying along with it, the eyelashes. The lashes rubbing the eyeball causes continous irritation and corneal ulceration.

Ectropion: Evertion of lid margin carries along with it puncta also and the presenting symptom is persistent watering from the eye-epiphora. Severe ectropion causes lagophthalmos (incomplete closure of eye lids and exposure of the cornea). This can lead to dryness of the eye and corneal ulceration (Fig. 48.10).

State of Lid Margins

Blepharitis is inflammation of lid margins. The eyelashes are glued by inspissated discharge. To expose the lid margin the crusted discharge should be soaked with wet cotton and wiped away. This may reveal redness and swelling of lid margins with ulceration in the root of eyelashes. When there is inflammation of meibomian glands, gentle pressure on the lid leads to extrusion of pus from their ducts. In seborrheic dermatitis affecting the scalp, the lid margin may show scales and signs of irritation. This is known as *squamous blepharitis.* As blepharitis progresses the eyelashes fall off leading to madarosis, i.e. loss of eyelashes.

Condition of Eyelashes

Normal eyelashes curve upwards smoothly. *Trichiasis* is turning in of eyelashes, so as to rub the eyeball. The eyelashes may undergo graying in elderly subjects. Pathological greying may develop in some cases of chronic uveitis occurring in sympathetic ophthalmitis and *Vogt-Koyanagi-*

Harada syndrome. It may also be part of vitiligo. Presence of extra row of eyelashes is known as *distichiasis*. This can give rise to foreign body sensation due to the inturned eyelashes. *Pediculosis* may affect the eyelashes and give rise to intense pruritus. Lice and their nits must be looked for in such cases.

Swelling along the Lid Margin

Painful swelling in the lid with edema is seen in hordeolum externum which is caused by acute inflammation of Zeiss glands and hordeolum internum which is caused by inflammation of meibomian glands (tarsal glands). The former tends to form abscesses close to the roots of eyelashes and the latter tend to burst through the conjunctival aspect of tarsus. Small painless swellings in the lids which are better felt than seen are suggestive of *chalazion* which is chronic granulomatous inflammation of the meibomian glands. Meibomian carcinoma presents as painless slow growing swelling close to lid margin. It is more common in the elderly. It is usually hard, immobile and associated with involvement of regional lymph nodes (Figs 48.11 and 48.12). Tumors occurring on the lids include neurofibroma, papilloma, melanoma, molluscum nodules, hemangioma and basal cell carcinoma. Xanthelasma present as soft, raised yellowish plaques appearing on the medial aspects of both eyelids. *Xanthelasma palpebrarum* used to be clinically associated with hyperlipidemia though the cause and effect relationship is only weak. Hemangioma occurring in the distribution of the trigeminal nerve may be associated with intracranial hemangioma and epilepsy *Sturge Weber syndrome*.

CONJUNCTIVA

Tarsal conjunctiva of lower lid is examined first by pulling down the lower lid. It is normally smooth and red. Lower fornix comes into view when the patient looks up with the lower lid gently everted. It is hyperemic in conjunctivitis. Presence of follicles which are small elevated nodules, foreign bodies, membrane and discharges are looked for. Adhesions between tarsal and bulbar conjunctiva may be seen as small bands connecting them—*synechia* (Fig. 48.13). Tarsal conjunctiva of upper lid can be exposed by everting it. For this the patient is asked to look down and the upper lid is gently grasped and pulled forward between the thumb and index finger. While pressing downwards at the upper border of tarsus with the index finger or a rod the lid is quickly everted (Fig. 48.9).

Lesions of trachoma, spring catarrh, follicles, foreign bodies, membrane and other abnormalities are looked for (Fig. 48.14).

The bulbar conjunctiva is examined next.

Normally it is transparent and the white sclera is seen through it. In conjunctivitis it is congested and hyperemic with dilated and tortuous vessels. Conjunctival congestion has to be distinguished from circumcorneal congestion. In conjunctival congestion, hyperemia is maximum at the fornix and it reduces towards the cornea. The dilated tortuous vessels can be made out clearly. On the other hand circumcorneal congestion is maximum around the



Fig. 48.11: Advanced meibomian gland carcinoma

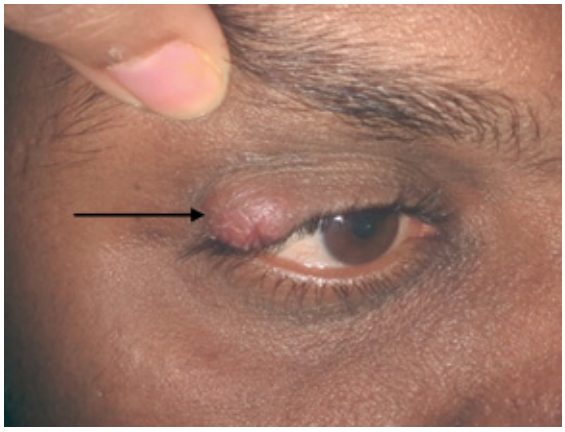


Fig. 48.12: Left eye hordeolum internum



Fig. 48.13: Symblepharon: Adhesion between conjunctiva of lid and eyeball often traumatic or burns

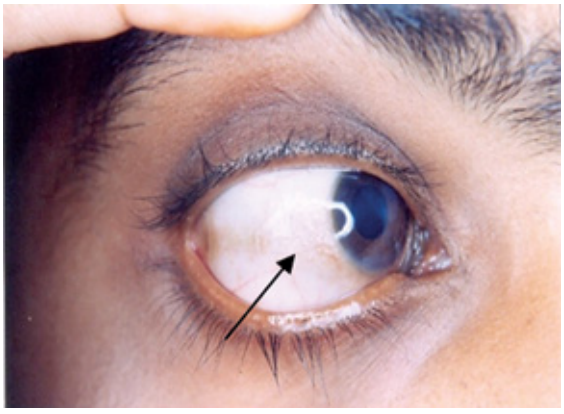


Fig. 48.15: Bitot's spot—shiny white spots on the conjunctiva in vitamin A deficiency



Fig. 48.14: Spring catarrah—gelatinous thickening-conjunctiva



Fig. 48.16: Left eye anterior staphyloma. Staphyloma is protrusion of the cornea or sclera often due to penetrating injury

Table 48.1: Features which distinguish conjunctival and corneal congestion

Conjunctival congestion	*Corneal congestion*
1. Bright red blood vessels	Ciliary congestion has a purplish tinge
2. Conjunctival vessels can be moved by moving them with the lower lid	Ciliary vessels cannot be moved
3. Individual vessels and the network can be seen	Separate vessels are indistinguishable
4. If blood vessels are emptied by pressure from limbus, the vessels fill slowly	Ciliary vessels fill rapidly

cornea and it reduces towards the periphery. Other features which distinguish conjunctival and corneal congestion are given in Table 48.1.

Chemosis is swelling of the conjunctiva. It occurs in allergic conditions and in orbital inflammations. *Phlycten* appears as a raised yellow nodule in the conjunctiva near the corneal margin. In membranous conjunctivitis bulbar conjunctiva shows membrane. Gelatinous thickening around the limbus is characteristic of the bulbar form of spring catarrh. *Bitot's spots* are whitish wrinkled raised patches of conjunctiva seen outside the lateral margin of the cornea. These occur in vitamin A deficiency (Fig. 48.15). Ulceration can occur rarely in various mucocutaneous disorders such as erythema multiforme.

CORNEA

Normal cornea is smoothly curved and transparent. Opacities, foreign bodies, vascularization, ulceration and distortion of its curvature are looked for. Protrusion of the central part of the cornea is a conical manner is known as *keratoconus* (Fig. 48.16). It leads to refractive errors. Thin opacity of the cornea is called *'macula'* and a dense opacity is



Fig. 48.17: Corneal ulcer. *Note:* Intense congestion, stainable opacity in the cornea and collection of pus in anterior chamber (hypopion)—(arrow)

called *'leucoma'*. Corneal ulcers and other nonulcerative lesions may cause severe pain and blepharospasm (Fig. 48.17). A foreign body in the cornea can be seen better with oblique illumination. Loss of corneal epithelium is demonstrated by fluorescein staining. One drop of 2% solution of fluorescein is instilled into the eye and the excess of the dye is washed with normal saline after two minutes. Areas devoid of epithelium take up green stain.

Vascularization of the cornea can be identified. This may be superficial and subepithelial or deeper to Bowman's membrane.

The points help to distinguish superficial from deep vascularization (Table 48.2).

Corneal sensation should be tested by touching with a wisp of cotton wool taking care not to touch the lids or lashes. This evokes reflex closure of lids—corneal reflex. Absence of corneal reflex indicates a lesion of the ophthalmic division of the trigeminal nerve. Larger size of the cornea in an infant is a very significant finding and it points to congenital glaucoma.

Table 48.2: Points to distinguish superficial from deep vascularization

	Superficial	*Deep*
Appearance of blood vessels	Bright red	Hazy and dull
Corneal epithelium	Raised and irregular Parallel vessels	Normal and smooth
Blood vessels on the surface	They can be traced to the conjunctiva	Usually vessels running from periphery to center. They can not be traced to the conjunctiva

Corneal Surface

Irregularities in curvature or smoothness of cornea can be made out by keratoscopy using the *Placido's disk*. This disk is 20 to 25 cm in diameter bearing alternate concentric black and white circles and provided with a central hole and handle. The observer looks through the central hole and observes the reflection of the disk on the cornea. Distortion of the circles indicates abnormalities of curvature and the surface.

Pigmentation

In keratoconus a brownish ring of pigment, probably hemosiderin, may form around the base of the cornea in advanced cases. Retention of any foreign body containing copper may lead to golden brown pigmentation in the deeper layers along the periphery of the cornea. A similar ring of pigment may be seen in Wilson's disease—*Kayser-Fleischer ring*. In *arcus senilis* a grayish ring appears just internal to the corneal margin leaving a rim of normal cornea at the periphery. Bleeding into the anterior chamber (*hyphema*) may lead on to brownish or greenish pigmentation of the cornea.

Keratic precipitates are seen as small spots of haziness in the deeper layers. This is best seen with the slit lamp.

Degeneration and loss of transparency of the cornea occurs in advanced deficiency of vitamin A. The cornea may ulcerate and melt away. This condition is called *keratomalacia*.

SCLERA

Sclera is examined for the presence of nodules, thinning, scleritis and episcleritis. Degeneration and perforation of the sclera with herniation of uveal tissue is called *scleromalacia perforans*. This occurs in rheumatoid disease.

ANTERIOR CHAMBER

It is examined next. Its depth is assessed. It is shallow in infants and in hypermetropes. It is deep in myopes. Excessive depth of anterior chamber is suggestive of absence of lens, i.e. *aphakia*. The depth of the anterior chamber is irregular in subluxation of lens. Presence of turbidity, blood or pus are looked for. Turbidity of aqueous humor is

indicative of active uveitis. It is confirmed by slitlamp examination. Presence of blood in the anterior chamber is known as hyphema and usually it follows trauma. It can also result from rupture of fragile vessels in cases of *rubeosis iridis* and tumors of the iris. Presence of pus in the anterior chamber is called *hypopyon.* It results from corneal ulceration and uveitis. The angle of the anterior chamber is examined in detail by gonioscopy.

IRIS

Iris is a circular vascular diaphragm pierced in the center by round opening the pupil. Abnormalities that we may see are:

- Structural abnormality of the iris
- Abnormal pupillary reactions

Structural Abnormalities of the Iris

Congenital abnormalities: Coloboma iris–Full thickness defect in the iris tissue reaching up to the pupil. Usually seen in lower part, often associated with coloboma of ciliary body, retina, optic nerve, etc.

Aniridia: Iris tissue absent except for a tiny rim often associated with glaucoma and Wilm's tumor of the kidney.

Aquired abnormalities: Inflammation of iris is usually associated with inflammation of ciliary body called iridocyclitis. Iridocyclitis causes many abnormalities like muddy iris (loss of anatomical markings), nodules in iris, irregular pupil due to inflammatory adhesion of pupillary margins to the lens (*See* Fig. 48.18).

Pupillary reflexes: There are three normal pupillary reflexes (See also Figs 32.9 and 32.10 A and B).

1. *Light reflex:* Pupil contracts when light fall on the eye actively. This is the direct light reflex. Pupil of the other eye also contracts (consensual light reflex).
2. *Near reflex:* Contraction of pupil occurs on looking at a near object—reaction of convergence and accommodation.
3. *Pschycosensory reflex:* Psychic and sensory stimuli (fear, anger and others) causes dilatation of pupil.

How to test the pupillary reaction?

Patient is comfortably seated in a low illuminated room. Patient is asked to look at distance to prevent accommodative constriction of pupil.

Note the size, shape and contour of pupil.

To elicit direct reaction to light: A focused and bright light is used to elicit the reaction. By slight lateral movements the light can be moved on and off the pupil—observe the pupillary reaction. Pupil remains contracted as long as the light is on.

To elicit consensual reaction: The observer keeps his hand over the nose in such a way as to separate the two eyes—throws light in one eye bringing it from side to the pupil and observes the other pupil for contraction. Normally both pupils contract on throwing light in one eye—this is consensual reaction.

To elicit reaction to convergence and accommodation: Patient is asked to look at a distance. A small object like pen is held 15 cm from the patient's nose and he is instructed to look at this object suddenly. The pupillary reaction is noted. Both pupils should normally contract.

Swinging flash light test: This is to detect unilateral optic nerve disease. A bright focused light is thrown into one eye, note the constriction—keep the light on for 2 to 3 seconds and suddenly transfer it to the other side. This is repeated several times-note the state of the pupil. Normally both pupils remain contracted. In case of optic nerve disease (because of less input through the nerve to the midbrain) when the light is thrown into the affected side both the pupils will dilate and swinging back to the normal side both pupils will contract. This is called *Marcus Gunn pupil.*

Abnormal Pupillary Reaction

1. *Absent light reflex:* Pupil fails to contract to light and is usually dilated also. It is seen in advanced stage of diseases like optic atrophy, total retinal detachement.
2. *Hemianopic pupil* (*Wernicke's pupil*)*:* Absence of pupillary reaction when light is thrown from hemianopic side.
3. *Argyll Robertson pupil:* Classically seen in cerebral syphilis where the pupil is *miotic and irregular, does not react to direct light, reacts to convergence and accommodation.* Rarely, it can occur in diabetes, multiple sclerosis and ciliary ganglion lesions.
4. *Tonic pupil (Adie's pupil):* Seen in *young women, usually unilateral,* slightly dilated. Reaction to light and accommodation sluggish.

5. *Hutchinson's pupil: Bilateral dilated pupil seen in severe head injuries due to tentorial herniation and brainstem compression.*
6. *Pinpoint pupil:* Seen in brainstem injury (pontine) and also in opium poisoning.
7. Irregularity of the pupil may result following iridocyclitis or injury to the iris (Fig. 48.18).

Heterochromia: Difference in color of iris of 2 eyes usually seen in Horner's syndrome where the affected eye has hypopigmentated iris (Fig. 48.19).

- Causes of hypopigmented iris are:
- Horner's syndrome,
- Wardenberg syndrome,
- Fuch's cyclitis.

Hyperpigmentation is seen in case of *retained iron foregin* body in the eye and in case of *melanomas involving the iris* and in *generalized melanosis of the eye-Nevus of Ota (Fig. 48.20).*

Rubeosis iridis: Abnormal new vessels are seen in:
1. Long standing diabetes mellitus,
2. Neovascular glaucomas,
3. Tumors of iris like malignant melanoma.

LENS

Lens is examined for transparency, presence of opacities and pigmented spots. To expose the lens fully, the pupil has to be dilated with homatropine. Cataract is the condition in which the lens becomes opaque. This may be partial or total. The location of the opacities also differ in different types of cataract (Figs 48.21 and 48.22). When a lens is dislocated, its free margin can be seen. Ophthalmoscopy and slit-lamp examination give further details.

Intraocular Pressure

Normal intraocular tension is 15 to 20 mm Hg. This can be estimated by digital tonometry (Fig. 48.23).

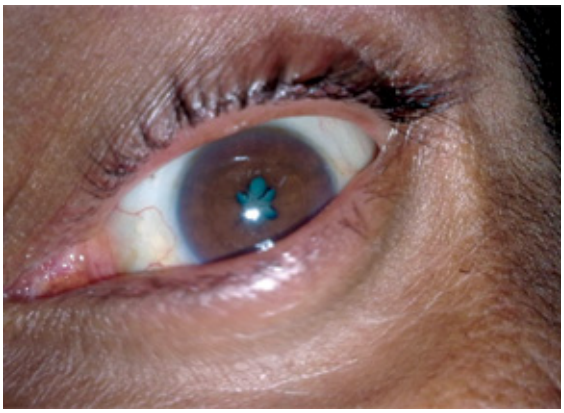


Fig. 48.18: Irregular pupil secondary to iritis



Fig. 48.20: Nevus of Ota. *Note:* Pigmentation of the sclera

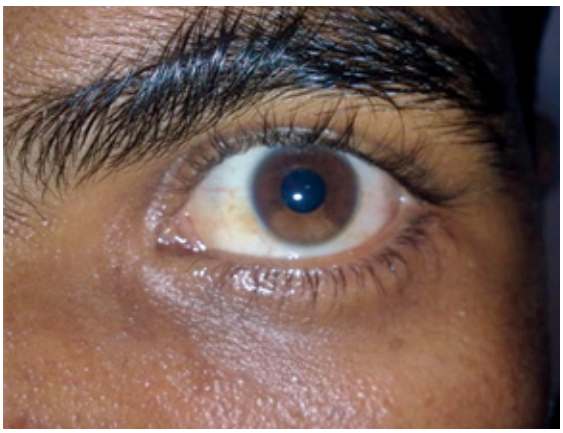


Fig. 48.19: Heterochromia iridum—left eye

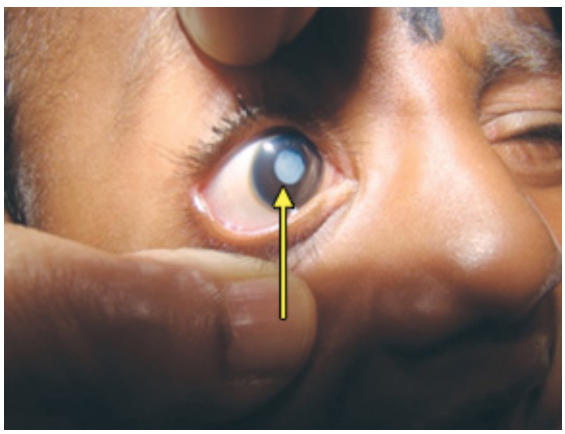


Fig. 48.21: Right eye congenital cataract (arrow). *Note:* Opacity of the lens – boy aged 7 years



Fig. 48.22: Left eye senile cataract (male aged—70 years)

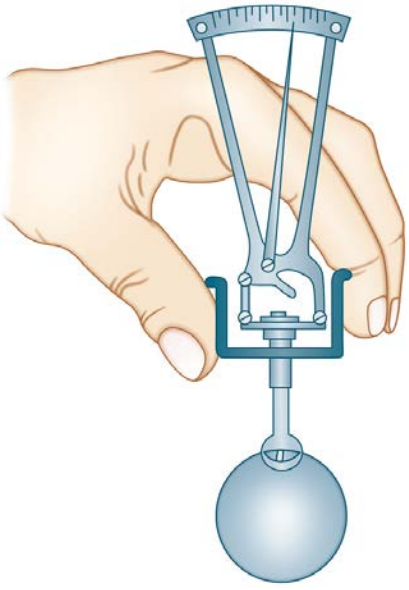


Fig. 48.24: Schiotz tonometer—used in measuring intraocular tension



Fig. 48.23: Digital tonometry to assess intraocular tension

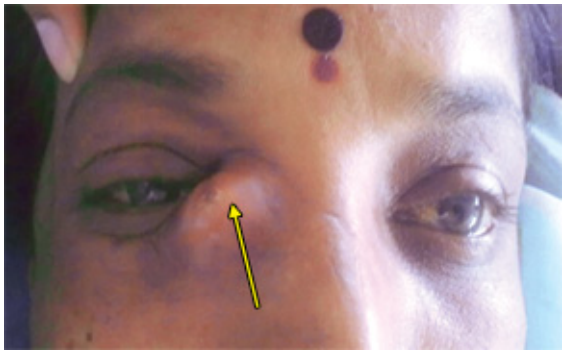


Fig. 48.25: Acute dacryocystitis. *Note:* Swelling at the medial end of the lower eyelid due to inflammation of the lacrimal sac (arrow)

Method

The patient is asked to look down. The sclera above the cornea is palpated through the upper eyelid. Both index fingers are placed above the tarsal plate and fluctuation is elicited. Rise in intraocular tension is assessed by the feel of the eyeball.

Intraocular pressure can be measured using a tonometer. The most reliable tonometer in clinical use is Goldman's Applanation tonometer which is more accurate than Schiotz tonometer (Fig. 48.24).

Lacrimal Sac

Look for swelling and tenderness. In mucocele of the lacrimal sac, pressure over the sac may lead to regurgitation of its contents through the puncta (Fig. 48.25). Rhinosporidiosis of the lacrimal sac presents as a boggy swelling over which the skin is stretched and appears shiny. This is known as the Rambo's sign.

OPHTHALMOSCOPY

(*See* also Section 11—Neurology, Chapter 32) Optic nerve head and retina can be inspected using an ophthalmoscope. Both direct and indirect ophthalmoscopy are available. In direct ophthalmo scopy the image of the retina is up-right, in indirect ophthalmoscopy, it is inverted.

Direct Ophthalmoscopy (Funduscopy)

The direct ophthalmoscope gives a direct view of the fundus and other structures of the eye. Opacities in the media and lesions of optic nerve and retina are seen with great accuracy and under a magnification of 15. Lesions of retina in front of the equator are not detected with this technique. When the media are hazy fundus details may be indistinct. These two defects are remedied to a great extent in indirect ophthalmoscopy.

Method

The direct ophthalmoscope is used with a positive 12 lens. Corneal and lenticular opacities are outlined against the red reflex of the fundus. The power of the lens in the ophthalmoscope is then reduced until the retina is in focus. The power of lens in the ophthalmoscope required to focus-up on the optic disk corresponds approximately to the patient's refraction.

Indirect Ophthalmoscopy

Binocular indirect ophthalmoscope is used in this technique. The principle involved is to make the eye highly myopic by interposing a strong convex lens of 14 0, 20 0 or even 30 0 between the examiner and the eye to be tested and sending in a powerful beam of light. A real inverted image of the fundus is formed between the observer and the convex lens. The image is magnified depending on the refraction of the eye, strength of the convex lens and its distance from the eye. With a lens of +13 0, the fundus of an emmetropic eye is magnified about 5 times. The powerful beam of light overcomes most of the opacities in the media. A larger portion of the retina including the periphery is brought into vision. Indirect retinoscopy helps to detect the peripheral lesions. Accessories like +90 d or +78 d lens used along with the slit lamp can also help seeing the central fundus—the disk and macula magnified about 5 times (Fig. 48.26).



Fig. 48.26: Indirect ophthalmoscopy

Appearances of Normal Fundus

Optic Disk

When the patient looks straight ahead the optic disk comes into view as the most prominent structure. It is pink in color and oval or circular in shape. The margins are sharp and there is a small depression in the center—the *physiological cup*. The central retinal vein and artery are seen to course over to the retina. These divide into the superior and inferior trunks at or near the surface of the disk. Each trunk divides further into temporal and nasal branches. The vessels should be followed in all the four quadrants as far as the equator, with patient looking in all the four directions.

The arteries are bright red and narrower than veins, which are purplish. The normal A-V ratio is 2:3. After examining the disk and the vessels, the macula is examined. A mydriatic may be instilled into the eye to faciliate proper examination, since light falling on the macula leads to pupillary constriction (Fig. 48.27).

Abnormalities detected by ophthalmoscopy:

1. Opacities in the media.
2. Abnormalities of optic disk.
3. Vascular abnormalities.
4. Hemorrhage.
5. Exudates.
6. Degenerative changes.
7. New growths.
8. Retinal detachment.
9. Several others (Figs 48.27 to 48.32).

Opacities in the Media

Irregularity of corneal curvature and opacities in the cornea and lens impair proper visualization of inner structures. In hypermetropia the disk appears smaller whereas in astigmatism it is distorted. Lens opacities appear as black spots against the red reflex and may cause the disk to appear more pink. Detachment of the vitreous appears as a circumscribed

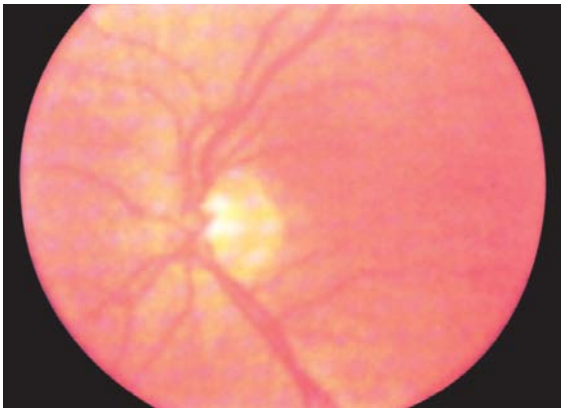


Fig. 48.27: Normal fundus. *Note:* The optic disk and macula

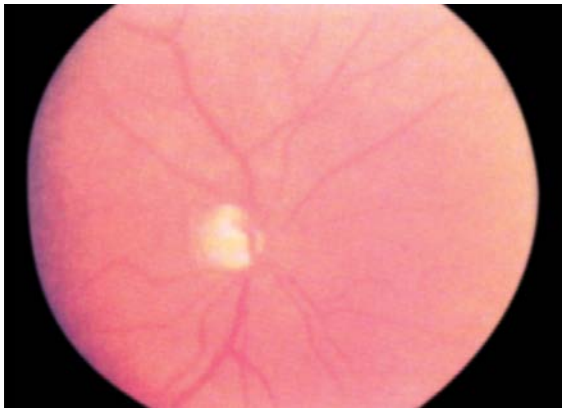


Fig. 48.29: Postneuritic optic atrophy

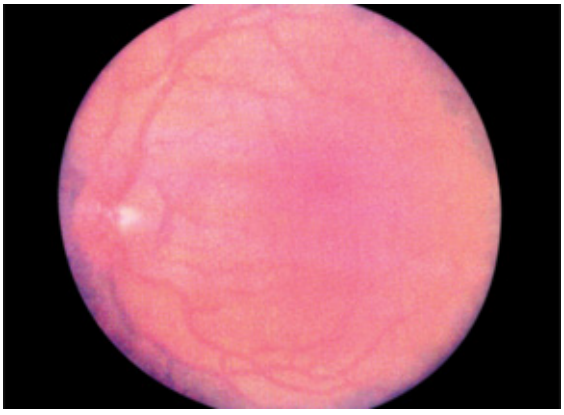


Fig. 48.28: Glaucomatous optic atrophy

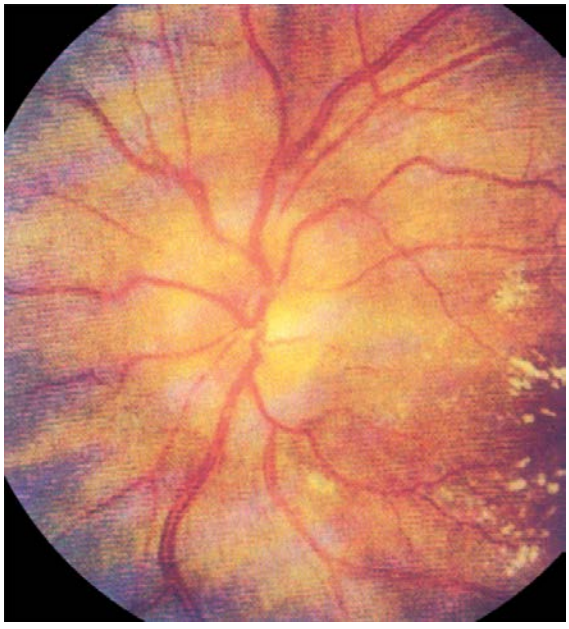


Fig. 48.30: Postpapilledemic optic atrophy

opacity in its posterior part. Cholesterol crystals appear as bright, and calcium soaps as gray round opacities. Erythrocytes, leukocytes, pigment cells and tumor cells appear as fine punctate opacities in the vitreous. Hemorrhage into the vitreous obstructs visibility.

Abnormalities of Optic Disk

Prominent abnormalities include glaucomatous cupping, optic atrophy, papilledema and papillitis.

Glaucomatous Changes

Earliest noticeable change is widening and deepening of physiological cup and nasal shifting of vessels. In longstanding glaucoma, the disk is pale, excavated deeply and the blood vessels appear kinked at the edge of the disk. There may be peripapillary choroidal atrophy.

Optic Atrophy

Optic atrophy results from degeneration of optic nerve fibers—*This may be primary optic atrophy, consecutive optic atrophy, glaucomatous atrophy or postneuritic and postpapilledemic optic atrophy*. The common feature is pallor of the disk. *Classification of optic atrophy is based on the fundus appearance and not on its etiology*.

Primary Optic Atrophy

Here the optic disk is almost normal in all aspects except in the color of the disk and the sharp margins. The disk is pale with atrophic cup. The vessels are

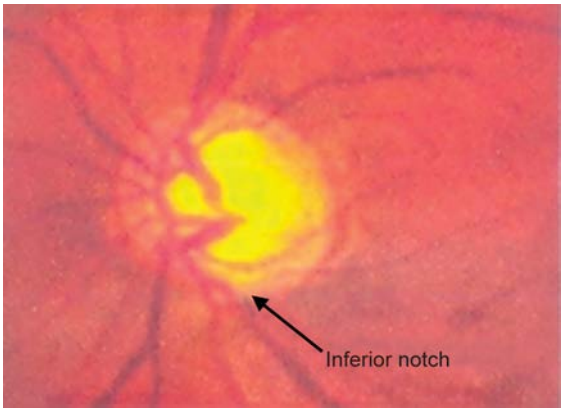


Fig. 48.31: Optic disk with inferior notch

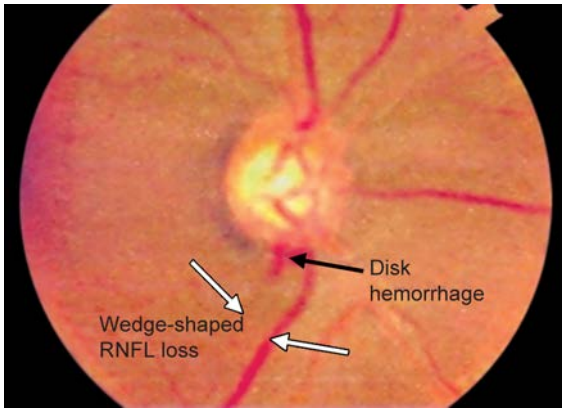


Fig. 48.32: Optic disk with disk hemorrhage

almost normal, but may be narrower slightly. Rest of the retina is normal.

Consecutive Optic Atrophy

This follows widespread degeneration of retina and is typically seen in retinitis pigmentosa and long standing occlusion of central retinal artery.

The disk is waxy pale, margins are blurred, vessels are markedly attenuated, and the physiological cup is obliterated. Sheathing of vessels may or may not be present.

Glaucomatous Optic Atrophy

It is seen in advanced glaucoma. The disk is very pale. The physiological cup is wide and deep. The blood vessels are kinked at the edge of the cup. The choroid around the disk shows atrophy and sclerosis-circumpapillary choroidal atrophy (Fig. 48.28).

Postneuritic and Postpapilledemic Optic Atrophy

These are indistinguishable from one another. The disk is pale, margins are blurred, physiological cup is obliterated, the vessels are sheathed on the disk and beyond (Figs 48.29 and 48.30).

Papilledema

Swelling of the optic disk leads to papilledema. Most frequently this results from conditions that raise intracranial pressure. Earliest evidence of papilledema is hyperemia of the disk and blurring of its margins, particularly the nasal. Edema gradually fills the physiological cup and spreads to the retina. The swelling can be measured by focussing on the disk with the positive lenses in the ophthalmoscope, and expressed in diopters (1 mm = 3 diopters). The retinal veins become extremely dilated and tortuous and the disk slowly mushrooms out with increasing edema. The disk margin becomes indistinct. Soft exudates and superficial hemorrhages occur in the posterior pole, particularly around the disk. Edema throws the internal limiting membrane into folds and this gives the appearance of macular fan or macular star. Vision may not be grossly impaired. Even in fully developed papilledema the vision can be 6/6. Longstanding papilledema leads to post papilledemic optic atrophy and visual loss (Fig. 48.30).

Pseudopapilledema

The appearance of the disk mimics papilledema. This may occur in high degrees of hypermetropia, astigmatism and opacities in the media which may make the disc appear hyperemic. Drusen embedded in the optic nerve may also mimic papilledma.

Optic Neuritis

Fundus picture may be indistinguishable from papilledema, but several differences exist.

1. *Vision:* In optic neuritis since the maculopapillary bundle is affected, sudden and profound fall of vision with a dense central scotoma is the rule. In papilledema vision is relatively retained till optic atrophy sets in.
2. Optic neuritis is usually unilateral whereas papilledema is often bilateral.
3. Swelling of the disk seldom exceeds 2 D in optic neuritis whereas in papilledema it may reach 6 to 8 D.

4. Optic neuritis is associated with fine vitreous opacities. Untreated cases progress to optic atrophy.

Blood Vessels

Arteries

Normally arterial blood column is seen through the transparent arterial wall and gives the appearance of the normal streak. Thickening of arterial wall leads to reflection of light. The streak becomes wider and appears as burnished copper—*copper wire arteries*. When the arteries are thickened further, they reflect all light and appear brilliantly *white-silver wire arteries*.

Sheathing: When the arteries are seen as white lines this is referred to sheathing.

Generalized narrowing of arteries occurs in hypertension arteriosclerosis, vasculitis from various causes, central retinal artery occlusion, toxic amblyopias, migraine and conditions that cause retinal degeneration.

Irregular narrowing appears as irregularity in size of the arteries. Constricted segments alternate with normal or dilated segments. These changes occur mainly due to endothelial proliferation of the intima.

Pulsation: Normally pulsations of arteries are not visible. Arterial pulsation at the disk is always pathological. This is seen in aortic regurgitation, aneurysms and thyrotoxicosis. Capillary pulsation can occur in aortic regurgitation and this is seen as alternating hyperemia and pallor of the disk corresponding to systole and diastole.

Veins

Congestion of retinal veins occurs in systemic diseases such as cardiac failure, polycythemia, chronic myeloid leukemia, hyperviscosity states, waldenstrom's macroglobulinemia and others.

Arteriovenous Changes

Normally the veins can be seen through the transparent arteries. In arteriosclerosis, loss of transparency of the artery obscures the vein. A thickened artery may press the vein at crossings and therefore the vein appears to be interrupted proximally and distended distally. This is called nicking. Sometimes the vein may be pushed aside at crossings. New vessels develop in longstanding venous occlusion and diabetes. This is called neovascularization.

Hemorrhages

Retinal hemorrhages are always pathological. When the hemorrhage is superficial it occupies the nerve fibre "layer and appears as striate or flame shaped bright red patches. When deeply placed, they appear as rounded irregular patches which are darker in color. When hemorrhage occurs between retina and the vitreous, i.e. preretinal or subhyaloid hemorrhage, usually the macular area shows it up as a large spherical reddish patch. It becomes hemispherical slowly due to settling down of erythrocytes.

Exudates

Soft exudates are spherical cottonwool-like patches in the retina. These are caused by microinfarcts and are seen in vasculitis and hypertension associated with renal disease. Hard exudates are irregular yellowish white patches or plaques usually seen around the macula. They are due to neuronal degeneration and lipid infiltration of the retina. They are seen in diabetes and arteriosclerosis.

Retinal Degeneration

Degenerative changes involve retina and choroid so that both the tissues are destroyed leaving the sclera bare. Pigment cells resist destruction and are seen scattered irregularly around degenerative lesions. Irregular patches of chorioretinal atrophy are seen in degenerative myopia, and in various types of choroiditis, retinitis pigmentosa, senile macular degeneration and occlusion of central retinal artery. In retinal degeneration the pigment is seen in front of the blood vessels whereas in choroidal lesions the blood vessels are seen to run in front of the pigment.

New Growths

Tumors may occur in the retina. These include retinoblastoma, angiomatosis, malignant melanoma, neurofibromatosis and others. Identification of these is by their appearance and further tests like fluorescein angiography.

Retinal Detachment

Simple detachment usually arises from retinal holes caused by degeneration. Early detection of these holes helps to institute prophylactic therapy. Secondary detachment results from tumor or excessive exudation from choroid. Traction bands stretching between retina and vitreous may develop as a result of recurrent vitreous hemorrhages and these may lead to retinal detachment. This is common in the proliferative stage of diabetic retinopathy.

FUNDUS CHANGES IN SYSTEMIC DISEASES

Diabetic Retinopathy

It is a leading cause of blindness. Major risk factors for diabetic retinopathy are blood glucose levels, high levels of glycolysated hemoglobin (HbA_{1c} > 7%), duration of diabetes and other comorbidities such as hypertension, pregnancy, smoking, chronic renal disease and others. Optimal medical control can reduce ocular complications.

Clinical Appearance

Diabetic retinopathy is classified into four groups:

1. Background retinopathy (nonproliferative) (Figs 48.33A and B)
2. Preproliferative retinopathy
3. Proliferative retinopathy
4. Diabetic maculopathy.

Background retinopathy: It is characterised by presence of dilated veins, deep retinal hemorrhages (dot and blot) microaneurysms, hard exudates, varying degree of retinal edema, scanty cotton wool spots.

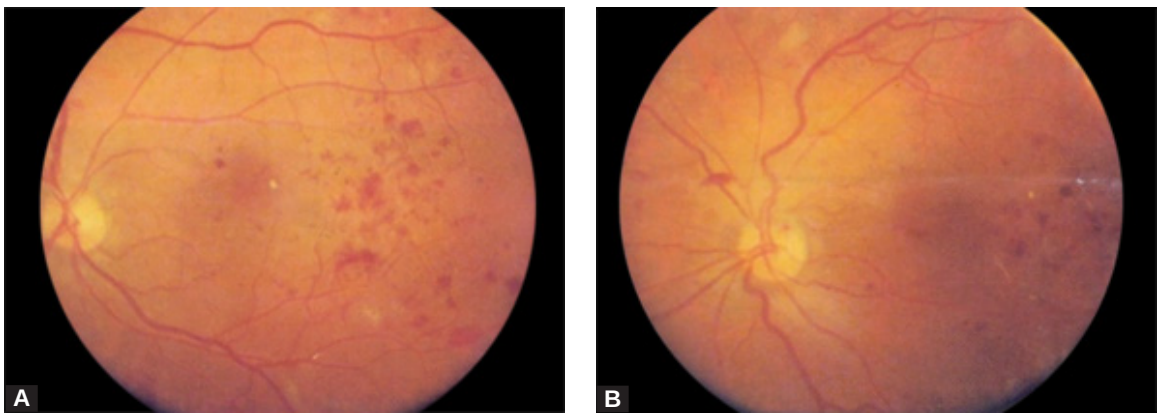
Preproliferative diabetic retinopathy: It represents more severe stage of background retinopathy. It is characterstized by intraretinal microvascular abnormalities (IRMA—dilated vessels within the retina). 10 to 50% patients with preproliferative retinopathy develop proliferative retinopathy within an year.

Proliferative retinopathy: It occurs in 5% of patients with diabetic retionopathy. New vessels grow on the surface of retina, optic disk and vitreous cavity. These fragile vessels bleed into the vitreous and retina leading to marked visual loss. Recurrent vitreous hemorrhages further leads to tractional detachment.

Diabetic maculopathy: It may be seen in any stage of retinopathy. It results from increased vascular permeability with or with out intraretinal lipoproteion deposits. It can also result from ischaemia due to closure of foveal capillaries.

Clinically significant macular edema (CSME) includes any of the following feature:

1. Thickening of retina at or within 500 micrometer of the center of the macula.
2. Hard exudates at or within 500 micrometer of macula.
3. Zones of retinal thickening one disk area or larger any part of which is one disk diameter of center of the macula (Fig. 48.34).



Figs 48.33A and B: Diabetic retinopathy—different stages (A) Severe nonproliferative diabetic retinopathy, (B) Moderate nonproliferative diabetic retinopathy with maculopathy. *Note:* Cotton wool patches, retinal hemorrhages are prominent. Vascular proliferation is less prominent in nonproliferative retinopathy. In proliferative neovascularization and abnormal new vessels will be evident

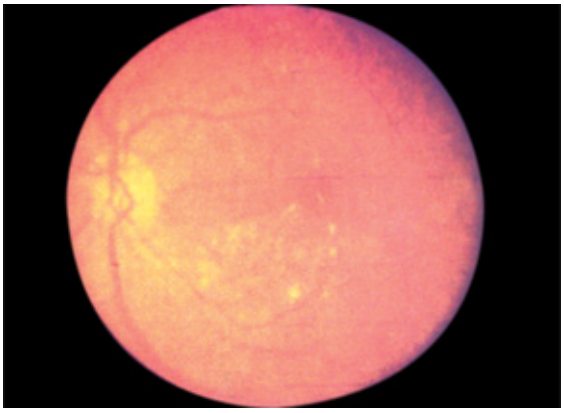


Fig. 48.34: Diabetic retinopathy. Note the exudates which are yellow and microaneurysms which appears as clear red dots

Hypertensive Retinopathy

Fundus picture of hypertension is modified to a great extent by coexistent arteriosclerosis. Young patients with mild to moderate hypertension may not show any fundus abnormality except narrowing and pallor of arterioles caused mainly by spasm. Superficial hemorrhages may be seen, but exudates are absent. When hypertension is associated with arteriosclerosis the caliber of the arteries is irregular with segments of constriction and dilatation. Sheathing may be present. Hard exudates may be seen particularly around the macula, but edema is absent.

In subjects with very high blood pressure levels as occurring in renal hypertension, proliferative and fibrous changes occur in the vessels making them narrow and tortuous with arteriovenous nicking. Soft exudates, edema, and superficial hemorrhages develop. Hard exudates in the macular area may give the appearance of macular fan or star. When hypertension enters the malignant phase, papilledema also develops. Papilledema, hemorrhage, soft exudates, edema and vasospasm regress when the blood pressure is controlled.

Toxemia of Pregnancy

The retinopathy of toxemia of pregnancy has many features similar to that of hypertension in young subjects. Earliest change is narrowing of the arterioles, particularly the nasal branches. If hypertension and albuminuria progress, exudates and hemorrhages appear in abundance. Exudative retinal detachment can occur.

Roth's Septic Retinitis

This is seen in cases of bacteremia or septicemia caused by infective endocarditis. The characteristic picture is the occurrence of retinal hemorrhages with white centers.

Retinitis Pigmentosa

The ophthalmoscopic picture is diagnostic. The disk is pale, yellowish or waxy hazy margins, and the vessels are markedly attenuated. Retina is studded with black pigment which starts initially at the equator. The pigment deposits resemble bone corpuscles in shape and affect the macula last. Other ocular abnormalities include myopia, keratoconus, complicated cataract and glaucoma. Clinical variants occur. In retinitis pigmentosa sine pigment—the disk is typical of the condition, but pigment spots are absent. In retinitis punctata albicans pigment spots are replaced by multiple white dots.

Retinopathy of Anemia

In severe anemia, the general fundus is pale, veins are dilated and hemorrhages with white centers may develop.

Retinopathy in AIDS 50 to 60% of patients suffering from AIDS show vascular and inflammatory lesions. Fluffy white spots or cotton wool spots are frequently seen in the posterior pole. These are caused by ischemia of nerve fiber layer. Superficial hemorrhages can also develop. Retinitis caused by opportunistic organisms like cytomegalovirus is common in the later stages. The retinitis is characterized by widespread necrosis of retina associated with profuse exudation, edema and hemorrhages.

Retinopathy of Prematurity

Retinopathy of prematurity (ROP) is essentially a proliferative retinopathy seen in premature infants. Two important risk factors for the development of ROP are:

1. Earlier gestational age (<32 wks) and
2. Low birth weight (1500 gm).
3. It also correlates with higher oxygen saturation caused by excessive oxygen administered to premature infants. Of late there is increase in the incidence of ROP.

Pathophysiology

Normal retina is gradually vascularized from optic disk to the periphery in the second half of gestation.

The nasal part of the retina grows up to the orra serrata by eight months and is vascularized. The temporal part grows up to the ora serrata only after term and so at birth, and especially in premature the temporal part is still immature and not fully vascularized. The earlier in the gestation period an infant is born, the less mature the retina. Excessive oxygen affects the developing vessels causing their obliteration. The peripheral vascular retina becomes hypoxic and releases humoral agents including vascular endothelial cell growth factor (VEGF) which stimulate growth of new vessels. This ultimately results in a picture resembling proliferative diabetic retinopathy.

REFRACTIVE ERROR

Normal eye can focus the image of objects sharply on to the retina to produce clear images. This is called emmetropia. When the optical system is abnormal the image is blurred—this condition is called ametropia. Ametropia results from alterations in the length of the eyeball, changes in corneal curvature, changes in the lens, and changes in refractive indices of the media. Of all these, axial length of the eye is most important. When the eyeball is shorter the image falls behind the retina as in hypermetropia and when the eyeball is longer, the image falls in front of the retina, as in myopia.

Hypermetropia

At birth the eyeball is shorter and hypermetropic. It develops to its normal length by the age of 3 to 4 years. On account of efficient accommodation by the lens, this defect is compensated and images still fall on the retina and produce clear images. If the eyeball does not grow to its normal length, hypermetropia results. Constant tension of the muscles of accommodation causes eye strain (asthenopia) and headaches, particularly after working with near objects for long periods. In children with hypermetropia accommodation to near vision which is associated with excessive convergence may lead to accommodation type of convergent squint. Hypermetropia can be corrected by convex lenses. Full correction is essential when accommodative squint is detected.

Myopia

Myopia leads to defect in distant vision. Increase in axial length of the eyeball of 1 mm causes myopia of 3 diopters. Generally myopia occurs as a congenital defect. It may be a simple growth variant as in simple myopia or may be progressive and pathological. Congenital myopia is due to abnormal length of the eye at birth, and it may be associated with other congenital anomalies. It seldom progresses. Simple myopia starts as school myopia, progresses slowly over years and stops when the growth spurt is over. It seldom exceeds 6 diopters and vision can be fully corrected with suitable concave lenses. Pathological myopia is associated with rapid progression which continues after puberty and the refractive error may reach up to 20 diopters. Atrophy and degenerative changes occur in the choroid and retina, resulting in the formation of retinal holes which predispose to retinal detachment. Such subjects should be followed up regularly with suitable visual correction and measures to prevent retinal detachment.

Astigmatism

Refractive errors caused by abnormalities in corneal and lenticular curvatures are known as astigmatism. Astigmatism is said to be regular when the two principal meridians of cornea are at right angles. Only regular astigmatism is amenable to correction with cylindrical lenses. Irregular astigmatism is caused by corneal scars and keratoconus.

PROPTOSIS

Proptosis is protrusion of the eyeball which may be bilateral or unilateral. Apparent proptosis (pseudoproptosis) may occur in conditions where eyeball is large as in buphthalmos or high myopia. Congenital bilateral proptosis usually occurs in oxycephaly. Acquired proptosis may be caused by orbital tumors or leukemias in childhood. In adults the most common cause is primary thyrotoxicosis.

Clinical Examination of a Patient with Proptosis

Progressive proptosis is a serious disorder which may lead to exposure keratitis, ulceration of the cornea and traction and compression of the optic

nerve, all leading to blindness. Degree of proptosis can be measured with *Hertel's exophthalmometer.* The distance of the anterior surface of the cornea from the lateral margin of the orbit should be measured.

Up to 20 mm	Normal
21-23 mm	Mild exophthalmos
24-27 mm	Moderate
Over 28 mm	Marked

Look for the following points:

a. Whether the proptosis is axial or eccentric
b. The eyeball is pulsatile or not—if it is pulsatile auscultate over it for bruits. Presence of pulsations and continuous bruit suggests caroticocavernous fistula.
c. Whether the proptosis increases with increase in venous congestion.
d. Ability to close the eyelids
e. Abnormalities of lids like edema, ecchymosis, or tumors.
f. Periorbital swelling and abnormalities in the neighboring structures
g. Abnormalities in the thyroid
h. Enlargement of preauricular and cervical lymph nodes
i. Diseases of paranasal sinuses and epistaxis.

The term *exophthalmic ophthalmoplegia* refers to the condition where the extrinsic muscles are rendered functionless due to severe exo-phthalmos. When proptosis leads to exposure keratitis, ulceration of cornea and blindness, it is called *malignant exophthalmos.*

Differential Diagnosis of Proptosis (Figs 48.35 and 48.36)

Inflammatory Causes

Common causes are orbital cellulitis and orbital osteoperiostitis. In orbital cellulitis, proptosis occurs rapidly with pain and signs of inflammation. The lids and periorbital tissues are woody hard and there is ophthalmoplegia.

Orbital Tumors

Rapidly growing tumors like rhabdomyosarcoma may also produce proptosis which may mimic inflammation because of their rapid progression and local signs of inflammation such as induration and reddish coloration of lids. Primary orbital tumors may arise from ocular structures, lacrimal gland, optic nerve or lymphatic tissue. Secondary tumors arise from adjacent sites and invade the orbit through the fissures and foramina or they may be distant metastases. Usually such tumors are slow growing and proptosis is unilateral. Orbital bones are commonly affected in different forms of histiocytosis.

In acute leukemias in children uni- or bilateral proptosis may develop and progress within weeks. In severe cases malignant exophthalmos may develop.

Primary thyrotoxicosis (Graves' disease) is associated with exophthalmos in the vast majority. Invariably bilateral, it can be unilateral and asymmetrical at times. The exophthalmos often



Fig. 48.35: Bilateral proptosis—Leukemia



Fig. 48.36: Proptosis right eye due to retinoblastoma

develops along with the thyrotoxic manifestations. Less commonly, it may precede the systemic manifestations or develop and worsen during, and after treatment of the thyroid lesion.

Pulsating exophthalmos is seen in carotico-cavernous fistula. There is enormous dilatation of vessels of lid and conjunctiva. The patient may complain of rumbling sounds and auscultation reveals bruit over the orbit. Retinal veins are congested, papilledema may be present and vision may be lost. Steady pressure on the globe reduces the proptosis. Compression of ipsilateral or contralateral common carotid artery tends to reduce the proptosis.

Intermittent Proptosis

In conditions like intracerebral arteriovenous communication and varicosity of orbital veins, compression of jugular veins may give rise to proptosis or increase an existing proptosis.

CHAPTER

49 Investigations in Diseases of the Eyes

N Vijayalakshmi Ammal, V Sujatha

General investigations, Fluorescein angiograhy, Computed tomography, Magnetic resonance imaging, Highly specialized office techniques in clinical practice, Ultrasonography, Corneal topography, Wave front analysis, Pachymetry, Specular photomicroscopy, Confocal microscopy, Optical coherence tomography, Electrical studies

GENERAL INVESTIGATIONS

1. Examination of urine—to detect diabetes mellitus and chronic renal disease
2. Routine blood counts, hemoglobin, ESR
3. Blood glucose, to exclude diabetes mellitus
4. Serology—to exclude syphilis, AIDS, and other infections
5. X-ray chest to exclude pulmonary tuberculosis
6. Mantoux test.

Special Investigations

Microbiological investigations of discharges from the eye and corneal scrapings—culture and sensitivity.

Radiology

Posteroanterior view of skull and special views for the orbit help to detect bony abnormalities like erosions, neoplasms, histiocytosis, fractures and the like.

Retinoscopy (Skiascopy or Shadow Test)

This is the most readily available method to estimate the condition of the refraction objectively. It is a specialist procedure.

Ophthalmodynamometry

This is the bedside method to measure ophthalmic artery pressure. It may be used to identify occlusive disease of the carotid system, which leads to pressure changes in the ophthalmic artery. Normal systolic pressure in the ophthalmic artery is 80% and diastolic pressure is 70% of the corresponding pressures in the carotid artery. A further reduction of 20% in systolic and 10% in diastolic pressure is suggestive of carotid artery occlusion.

FLUORESCEIN ANGIOGRAPHY

Fluorescein is readily bound to albumin in the bloodstream. Normal retinal-blood barrier prevents dye leakage and this delineates the retinal vessels of all calibers. In the choroidal circulation the dye passes freely across the endothelium of capillaries to the extravascular space. It cannot pass through the intact Bruch's membrane which lines the inner surface of the choroid and retinal pigment epithelium. About 3 mL of 20%, or 5 mL of 10% sodium fluorescein is injected into the antecubital vein as rapidly as possible. Photographs are taken at intervals of 6 to 8 seconds with a retinal camera after an initial delay of 9 seconds, and late photographs are taken after 20 minutes (Fig. 49.1).

When the dye enters the eye there is at first a choroidal blush, then it goes through retinal arterioles, capillary bed, and into the veins. Fluorescein angiography has diagnostic and therapeutic value. It is particularly useful in detecting diabetic retinopathy.

Fluorescein angiogram detects and localizes retinal vascular abnormalities, leaking vessels, and defect in Bruch's membrane and pigment

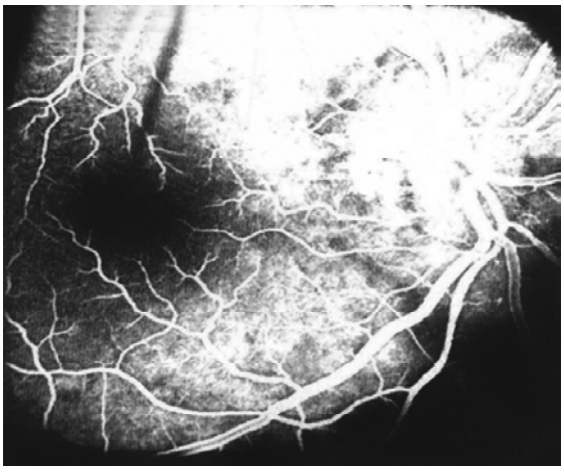


Fig. 49.1: Fundus fluorescein angiography showing the filling of retinal vessels



Fig. 49.3: CT scan showing bilateral proptosis and marked enlargement of extraocular muscles (arrows)



Fig. 49.2: Normal CT Scan. Note the normal position of the eyeball to extraocular muscle (arrowhead) and optic nerve (arrow)

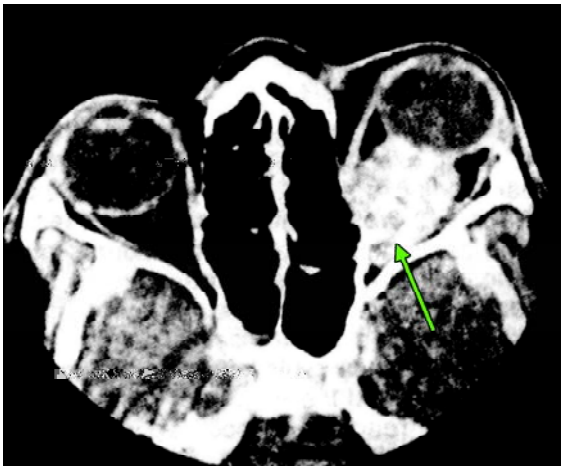


Fig. 49.4: CT scan showing proptosis left eye due to glioma of optic nerve (arrow)

epithelium. Fluorescein angiography is absolutely necessary to locate lesions before undertaking photocoagulation or laser therapy of retina. It also helps to study papilledema and to distinguish it from pseudopapilledema.

COMPUTED TOMOGRAPHY

It delineates the bony orbit, structures inside the eyeballs, optic nerve, muscles and soft tissue. Computed tomography (CT) has become the most important and useful investigation for orbital diseases, particularly tumors, thyroid ophthalmopathy and injuries. The combination of axial (CAT) and coronal (CCT) pictures gives three dimensional visualization of orbital lesions. CT scan with contrast medium further enhances the orbital shadows of certain orbital tumors. CT scan of the orbit gives exact site and size of lesion, involvement of adjacent structures like bony erosions and intracranial extensions if any (Figs 49.2 to 49.4).

MAGNETIC RESONANCE IMAGING

MRI can distinguish between abnormal and normal tissues and has excellent image resolution—axial, coronal and sagittal. T1 weighted images provide details of intraorbital structures like extraocular *muscles and optic nerve* which have a high intensity and brightness from fat. In T2 weighted images the vitreous appears bright and helps delineation of orbital structures.

HIGHLY SPECIALIZED OFFICE TECHNIQUES IN CLINICAL PRACTICE

Sophisticated techniques are now available to study the ocular tissues in great detail and precision enabling ocular evaluation at a cellular level. Some of these are:

- Ultrasonography
- Corneal topography
- Wave front analysis
- Pachymetry
- Specular photomicroscopy
- Confocal microscopy laser scanning microscopy OCT (optical coherence tomography).

Ultrasonography

Diagnostic ocular ultrasonography (USG) detects intraocular abnormalities when opaque media hinders proper examination. The information obtained is comparable to scan (Figs 49.5 and 49.6).

Advantages of ultrasonography over CT scan are:

- It provides similar information as CT.
- It is a dynamic examination allowing several views on a moving globe.

Forms of USG

- A scan
- B scan
- Ultrasound biomicroscopy (UBM).

A scan: One dimensional of time amplitude representation of echos received along the beam path. The distance between echo spikes is recorded along the oscilloscope screen and provides an indirect measurement of tissue such as globe length and lens thickness. A scan is mainly used to calculate the power of IOL to be implanted in the eye.

B scan: Echos produced are represented as dots inside of spikes. By the use of scanning techniques the dots are integrated to produce an echo representation of a two dimensional section of the eye. It is very useful to detect the intraocular tumors in children like retinoblastoma, vitreous hemorrhage, retinal detachment and others.

Ultrasound Biomicroscopy

Ultrasound biomicroscopy (UBM) is newer and more sensitive technique using high frequency transducer. This detects anterior segment pathology in great detail—cornea, iris, angle, lens and ciliary body.

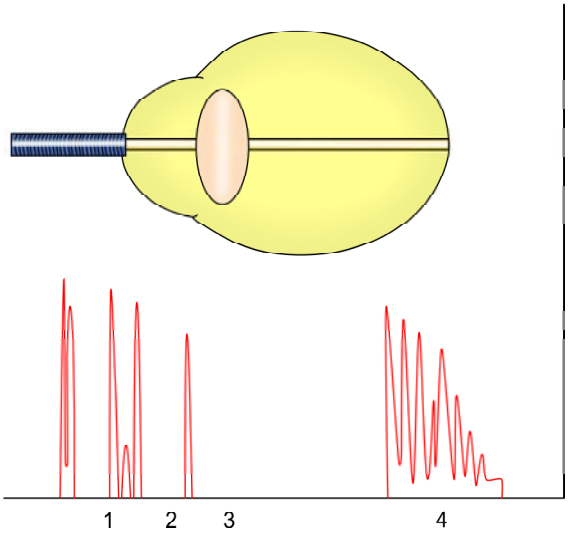


Fig. 49.5: High quality spikes by A scan. *Note:* Spike height should be of good amplitude. Spikes araising from the cornea, anterior surface of the lens, posterior surface of the lens, and retina are numbered 1,2,3 and 4

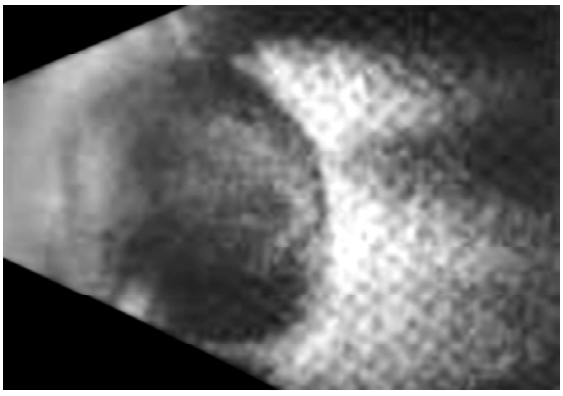


Fig. 49.6: Plenty of point like echoes in the vitreous cavity suggestive of vitreous hemorrhage

Ultrasound Evaluation of the Posterior Segment of the Eye

A and B scan biometry: Biometry is the process of measuring the power of the cornea (keratometry) and the length of the eye, and using this data to determine the ideal intraocular lens power. If this calculation is not performed, or if it is inaccurate, perfect correction of refractive error may not be possible. Several other functions can be performed by these scans.

Corneal Topography

It is a computerized mapping of color coded dioptric contour of the cornea. It is a video capture and analysis of concentric circle, placido disk images to produce videokeratographs. It is a very useful technique to locate steepest and flattest meridian of cornea and can detect subtle variations of power. Cool colors are lower in power than warm colors.

- Blue—flat
- Red—steep
- Green—normal

Corneal modeling system analyses 32 rings and 256 points—each ring having a power change resolution of 0.25 D. Corneal topography is very useful in screening patients for keratoconus and in the preoperative evaluation of refractive surgery patients.

Wave Front Analysis

Eye has many aberrations, each affecting quality of vision. Conventional refractive surgery does not address higher order aberrations or irregular astigmatism of the optical system. Wave front analysis is currently being used in wave front guided ablations to enhance vision in refractive surgery patients.

Pachymetry

Pachymeters measure corneal thickness. Normal corneal thickness is 0.52 to 0.54 mm in the center, 0.65 to 0.67 in periphery. Optical pachymeters are attached to slit lamp. More sophisticated equipments are now available to measure corneal thickness like orbscan corneal topographer (OCT) and pentacam camera.

Specular Photomicroscopy

This is a slit lamp like instrument which is camera mounted and gives clear view of endothelial cells of cornea. Normal endothelial cell count at birth is 2400 cells/mm^2. The count decreases with age. Abnormal shape of the cells and decrease of the number below normal limit will cause loss of normal endothelial function of keeping the cornea transparent.

Confocal Microscopy

This allows clear high resolution magnified view of corneal cells, structure of cornea, organisms infecting cornea like acanthameba, fungi and bacteria. Traditionally confocal microscopy is used to follow healing after refractive surgery or traditional surgery. Two different types of confocal microscopes are available:

1. Confocal slit scanning microscope
2. Confocal laser scanning microscope.

Confocal Slit Scanning Microscope

It is a diagnostic instrument that combines a confocal microscope and a precision pachymeter. Confocal laser scanning microscope has a high resolution 670µ diode laser. It is modified Heidelberg retinal tomography (HRT). It can scan an area 1µ × 400 µ with a magnification of up to × 800 and resolution of 1µ. With it's high depth resolution optical sections of only a few micrometers can be imaged with a rate of 30 frames per second. It is a valuable tool in evaluation of all anterior segment structures.

Confocal Laser Scanning Ophthalmoscopy

Topographical images of retina and optic nerve are created by focusing 670 nm laser beam on to these structures. Optic disk parameters like cup area, cup volume, CD ratio, rim volume, and nerve fiber layer thickness at peripapillary region can be calculated in the computer data system.

Optical Coherence Tomography

Optical coherence tomography (OCT) is a noncontact noninvasive high resolution cross sectional imaging technique which can measure tissue thickness with micron scale sensitivity. It uses infrared light waves 40 micrometer coherent light to penetrate the tissue and reflected images are caught on a camera. Image shows colors that corresponds to the reflectivity of the tissues. Highly reflective tissues like retinal pigment epithelium and nerve fiber layer are shown as red or white, while photo receptors and choroid are shown blue or black. Linear cross section of tissue is obtained when the scans are put together. Two forms of OCT are available.

Stratus Optical Coherence Tomography

This standard OCT performs 4 to 6 mm long radial line scans through retina or optic nerve. This gives information of retinal thickness, nerve fiber layer thickness, glaucoma status, and macular thickness.

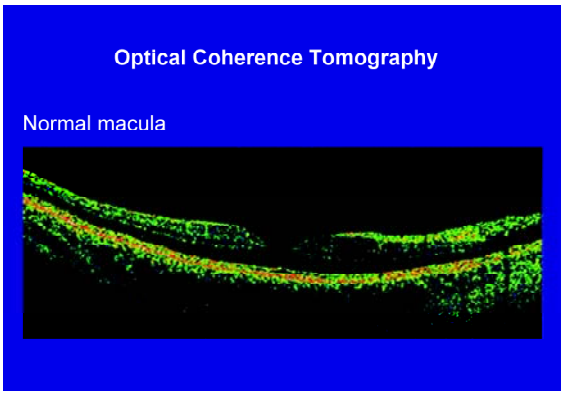


Fig. 49.7: Normal macula seen by OCT-showing all layers of retina with normal foveal contour with foveal depression

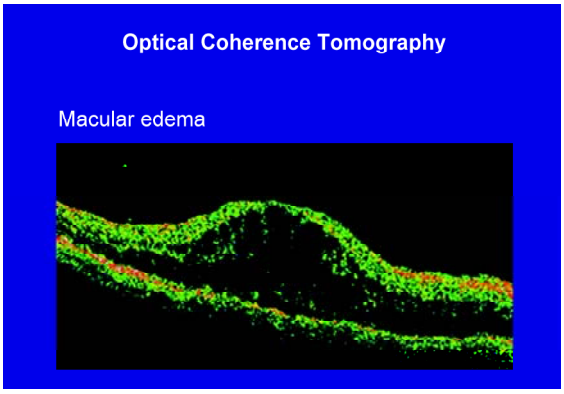


Fig. 49.8: OCT showing macular edema spongy edema involving inner retinal layers and loss of foveal contour

Stratus OCT is particularly useful in the assessment of macular lesions like macular edema, macular hole, epiretinal membrane and vitreoretinal traction (Figs 49.7 and 49.8).

Visante Optical Coherence Tomography

This is a new type of OCT for evaluation of anterior segment particularly cornea. This is useful in evaluation of cornea before and after refractive surgeries and keratoplasty.

ELECTRICAL STUDIES

Electroretinography

Electroretinography (ERG) is a record of electrical changes induced in retina by a light stimulus. Three components of the ERG are:

1. A negative 'a' wave representing the activity of rods and cones.

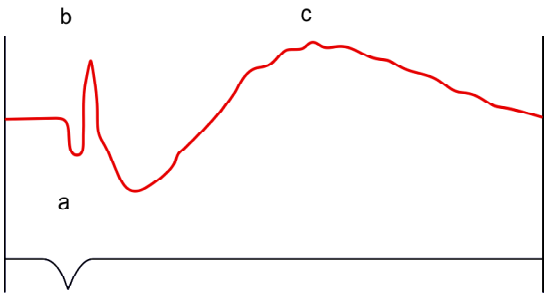


Fig. 49.9: Normal ERG

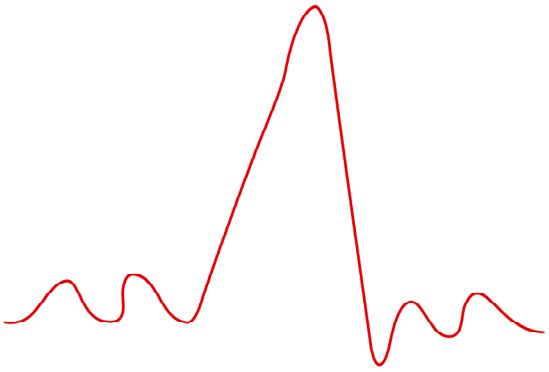


Fig. 49.10: Normal visual evoked response (VER)

2. The 'b' wave arising from the inner retinal layers.
3. The 'c' wave associated with the metabolism of the pigment epithelium (Fig. 49.9).

The response is extinguished in the conditions of gross destruction of rods and cones, like in primary retinitis pigmentosa and central retinal artery occlusion. The rod response is tested in dark adapted eye (scotopic ERG) and cone response in bright light (photopic ERG). Pattern of the ERG indicates activity of macula.

Visual Evoked Potentials or Visual Evoked Response

This is the visual response to specific alterations in the electroencephalogram by sensory stimuli. The response may be a flash VER to a flash of light or pattern reversal VEP—a fovea specific response (Fig. 49.10).

Flash VEP gives a gross assessment of integrity of macula or optic nerve.

Pattern reversal VEP is a fovea specific response as it depends on form sense and may give a rough estimate of visual acuity.

CHAPTER

50 Ophthalmic Emergencies

N Vijayalakshmi Ammal, V Sujatha

Acute congestive glaucoma, Injuries, Burns of the eyes, Causes of sudden loss of vision, Red eye

Several eye diseases require emergency treatment, blindening diseases like ophthalmic injuries, corneal ulceration and iridocyclitis have to be treated early to prevent visual loss. If infections of the cornea are not treated promptly, corneal opacities will develop. Similarly in uveitis, profuse exudation may block the pupil and lead to posterior synechiae and further complications.

Among the ophthalmic emergencies acute congestive glaucoma, injuries and the other causes of sudden loss of vision are more important.

ACUTE CONGESTIVE GLAUCOMA

This affects patients around the age of 50 years, more commonly women, who have hypermetropia with smaller eyeballs and shallow anterior chamber. The condition ushers in with severe headache, neuralgic pain and vomiting. Prostration develops early. The eyes are red and the lids are edematous. The cornea is hazy due to edema, the anterior chamber is shallow and the pupil is dilated and vertically oval. The eyeball is stony hard.

Management

1. Hospitalize the patient.
2. Administer analgesics like morphine 15 mg or pethidine 100 mg by 1M injection.
3. Acetazolamide (Diamox) 500 mg initially and thereafter 250 mg orally to be repeated 6 hrs later.
4. Osmotic agents such as 20% mannitol 200 mL as rapid IV infusion.
5. Instill 2 to 4% pilocarpine drops hourly into the eyes, so as to keep the pupil constricted maximally—This may help to open up the angle of the anterior chamber.
6. With the above measures intraocular pressure is usually brought to normal. Curative treatment is essentially surgical. If gonioscopy reveals extensive peripheral anterior synechiae, filtration operation has to be done. If they are minimal, iridectomy will suffice.

INJURIES

Both blunt and penetrating injuries require immediate attention.

Blunt Injuries

Blunt injuries may range in severity from sub-conjunctival hemorrhage to rupture of the eyeball. Rupture of blood vessels in the iris or ciliary body may lead to collection of blood in the anterior chamber or the vitreous. Bleeding into anterior chamber leads to secondary glaucoma. Blood staining of the cornea results in permanent opacification of its posterior surface.

Management

1. Keep the patient in bed
2. Acetazolamide orally 500 mg to 1 g orally 8 hourly helps to lower intraocular pressure. If the blood fails to be absorbed evacuate it by various surgical procedures.

Traumatic Dislocation of the Lens

Dislocation of the lens into the anterior chamber leads to two major complications:

1. It damages the corneal endothelium leading to permanent opacity.
2. The globular lens blocks the angle and produces secondary glaucoma.

The eye can be saved only by removing the lens after controlling the intraocular pressure.

Management

Remove the lens after controlling raised intraocular pressure by medical means.

Penetrating Injuries

These are always serious. There is always the risk of developing intraocular sepsis and retention of foreign bodies inside the eye.

Management

1. Assess the extent of injury by slit-lamp examination taking particular care to detect retained foreign bodies.
2. USG B scan is useful in detecting the damage to the posterior segment structures.
3. Meticulous repair of the wound is required.
4. Administer appropriate antibiotics systemically and locally in the eye.
5. Administer appropriate anti-inflammatory drugs such as prednisolone 10 mg qid or an NSAID (indomethacin) 25 mg qid orally.
6. Mydriatics like atropine have to be instilled into the eye to paralyse the iris.

Most often patient needs further surgical procedures to deal with complications.

BURNS OF THE EYES

This may result from fire accidents, as a part of general burns or may be caused by caustic chemicals falling into the eye, e.g. lime, acids, alkalies and other chemicals.

Management of Burns of the Eyes

Care should be taken to examine the eyes particularly when the lids are also affected. It is useful to instill local anesthetic drops before examination. Careless or hasty examination may cause not only pain but also damage to the already injured skin. Without wasting time, the eyes should be lavishly irrigated with sterile normal saline or 1% sodabicarb solution or at least with tapwater if the sterile solutions are not handy. Ideally weak acids are used to irrigate in cases of alkali burns and weak alkalies for acid burns. Using retractors the eyeball should be examined carefully and any particle like piece of lime or cement should be removed. If corneal epithelium has been lost, atropine or a weaker mydriatic should be instilled along with antibiotic drops. If conjunctiva has been burnt as evidenced by its dry, pale appearance, attempt should be made to prevent adhesion of opposing surfaces of raw conjunctiva and lids. For this, an antibiotic ointment should be applied in the conjunctival sac in sufficient quantity and a glass rod passed along the fornix all around to break adhesions. This maneuver may have to be repeated. Local application of steroids reduces scarring and adhesions but this has to be used with care.

CAUSES OF SUDDEN LOSS OF VISION

See Flow charts 50.1 and 50.2.

Major causes of sudden loss of vision include:

1. Acute congestive glaucoma
2. Central retinal artery occlusion
3. Optic neuritis and retrobulbar neuritis
4. Retinal detachment
5. Vitreous hemorrhage
6. Miscellaneous conditions, e.g. sudden development of diabetic cataract, spontaneous dislocation of lens into anterior or posterior chamber as occurring in Marfan's syndrome, hemorrhage in the macula, occlusion of central retinal vein and rapid development of corneal edema in keratoconus (hydrops cornea).

Central Retinal Artery Occlusion

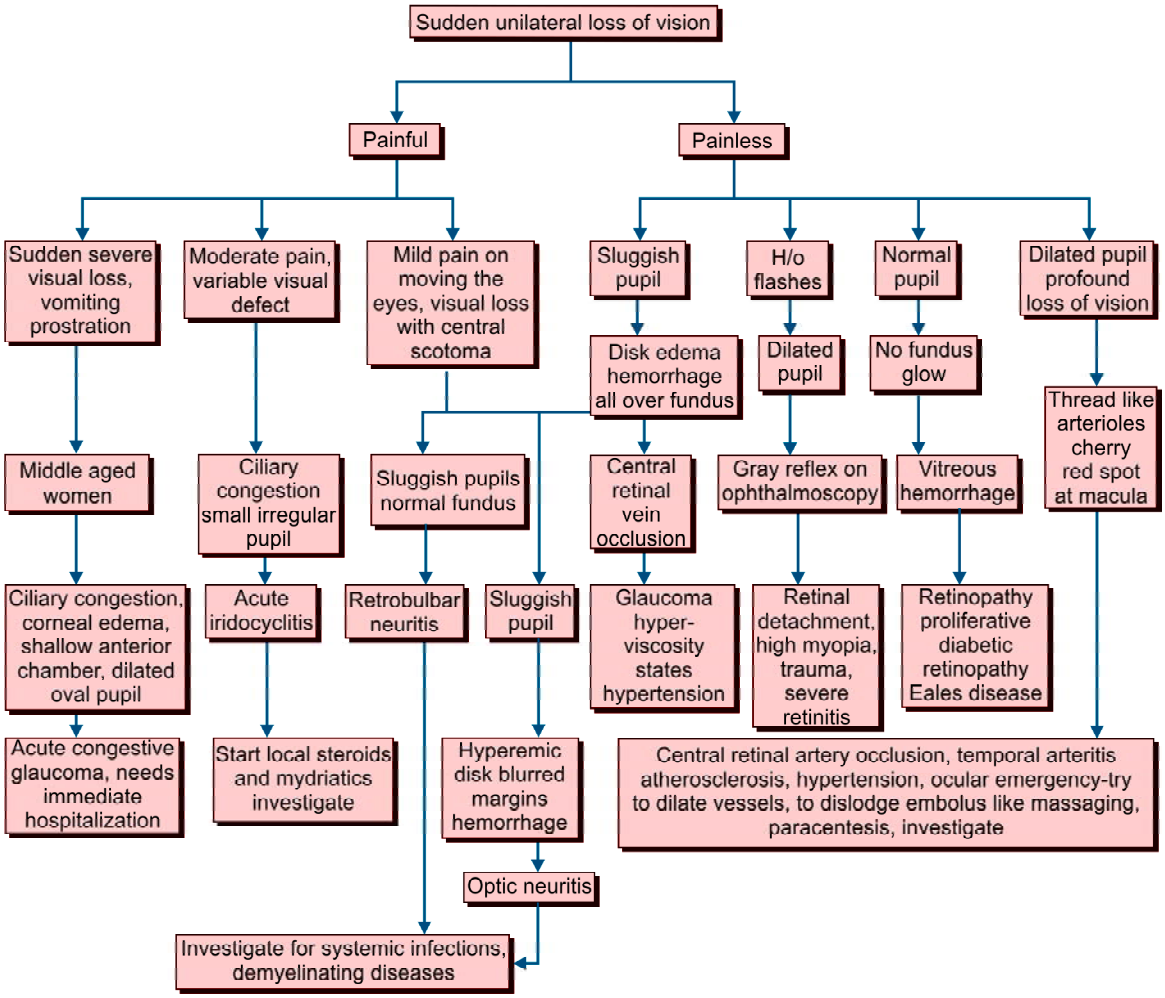
Most cases of central retinal artery occlusion come under observation after a lapse of hours or days. If the patient reports early, measures to dilate the retinal vessels are indicated in an attempt to dislodge the thrombus.

RED EYE

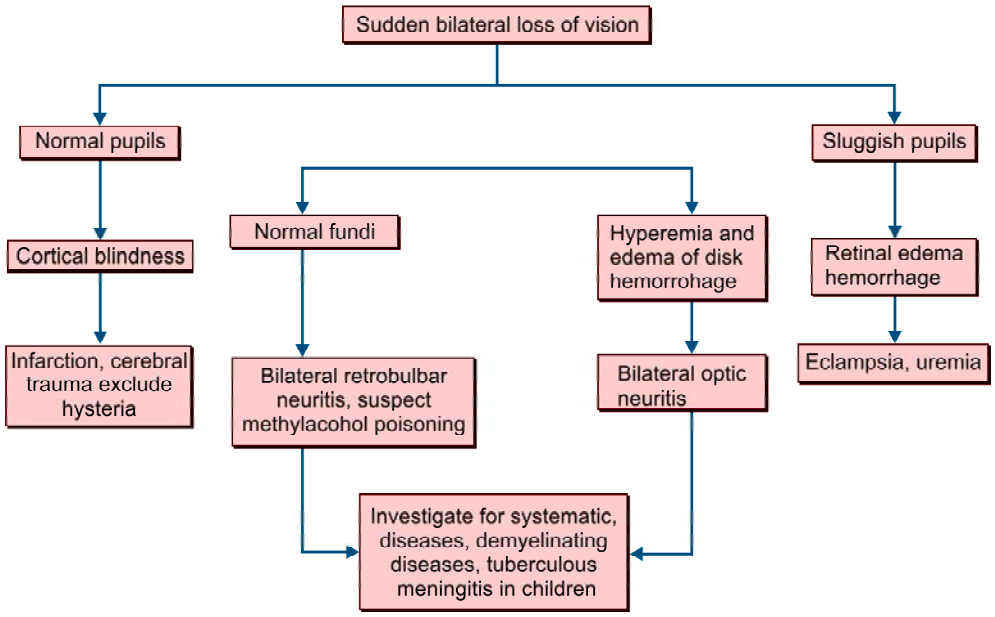
Some conditions give rise to unilateral or bilateral red eye. These accounts for many cases of eye problems in all general medical services. The

common conditions include simple problems like acute conjunctivitis, allergic conjunctivitis, spring catarrh, and subconjunctival hemorrhage and more serious problems such as iridocyclitis, scleritis and acute congestive glaucoma. The latter demand specialist cast for management. Flow charts 50.3 and 50.4 give details to assess the condition and plan management.

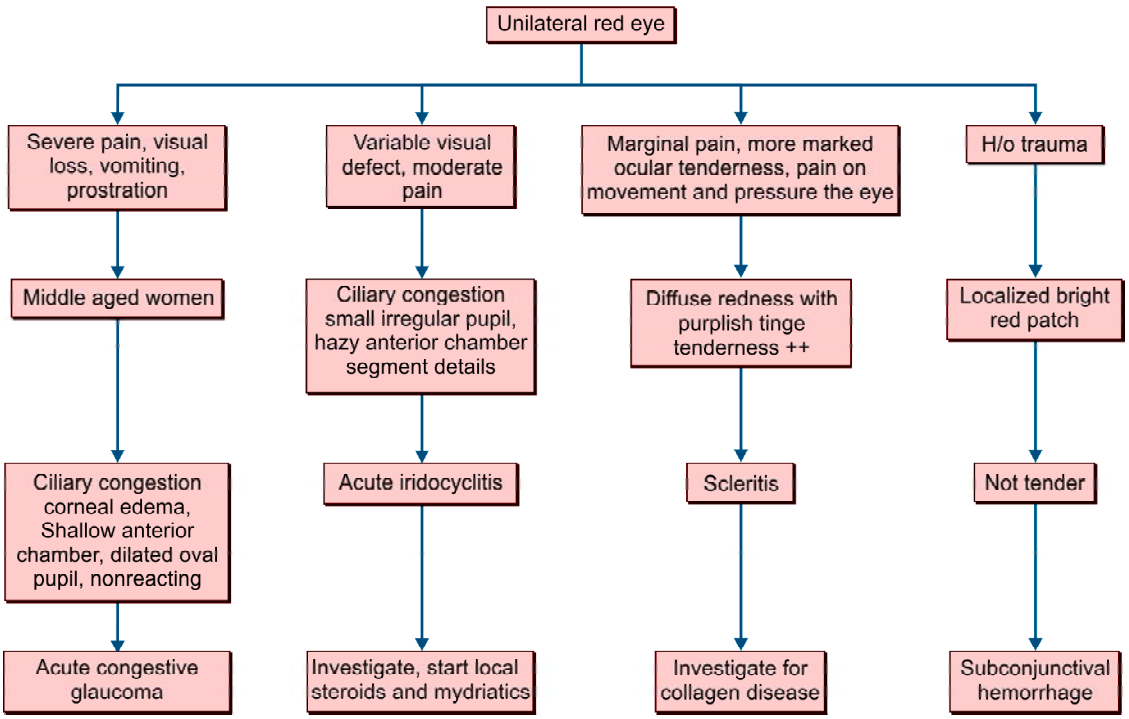
Flow chart 50.1: Sudden unilateral loss of vision



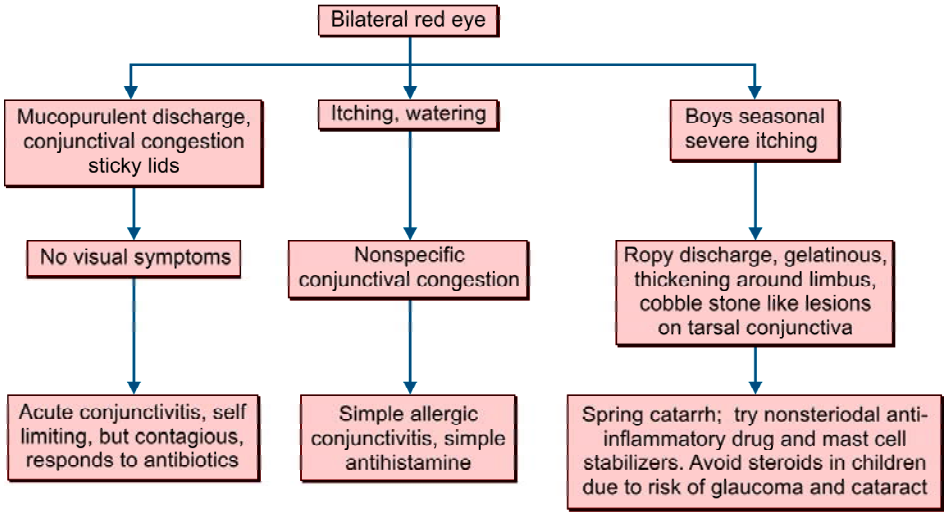
Flow chart 50.2: Sudden bilateral loss of vision



Flow chart 50.3: To diagnose unilateral red eye



Flow chart 50.4: To diagnose bilateral red eye



SECTION

18

Ear, Nose and Throat

CHAPTER

51 Otorhinolaryngology: General Considerations

OS Radhakrishna Pillai

General considerations, Anatomy of the ear, Physiology, Anatomy of the nose and paranasal sinuses, Anatomy of pharynx, Anatomy of larynx

GENERAL CONSIDERATIONS

Diseases of ear, nose and throat are day-to-day problems in general practice, accounting for 10% or more of the total attendance in any general hospital out patient service in India. A patient may present with acute symptoms like severe pain in the ear, vertigo, sudden deafness, epistaxis, unbearable pain in the throat and stridor; or chronic symptoms like ear discharge, progressive deafness, nasal block, nasal discharge, dysphagia and hoarseness of voice. The primary care physician has to manage most of these patients himself and refer only those who require specialized services to the ENT surgeon.

A short description of the applied anatomy and physiology of ear, nose pharynx and larynx is given below.

ANATOMY OF EAR AND PHYSIOLOGY

Ear, which is the organ of hearing and equilibrium is divided into three parts, the external ear, the middle ear and internal ear. The external ear consists of the pinna and the external auditory meatus. The external auditory meatus is cartilaginous in its outer 1/3 and bony in its inner 2/3 (Figs 51.1 and 51.3).

The skin covering the cartilaginous part contains ceruminous and pilosebaceous glands and hence this part may be seat of furuncles. The cartilaginous part is directed upwards and backwards while the bony part is directed downwards and forwards. In order to see the tympanic membrane, the pinna has to be pulled upwards and backwards to bring the two parts of external auditory meatus into alignment.

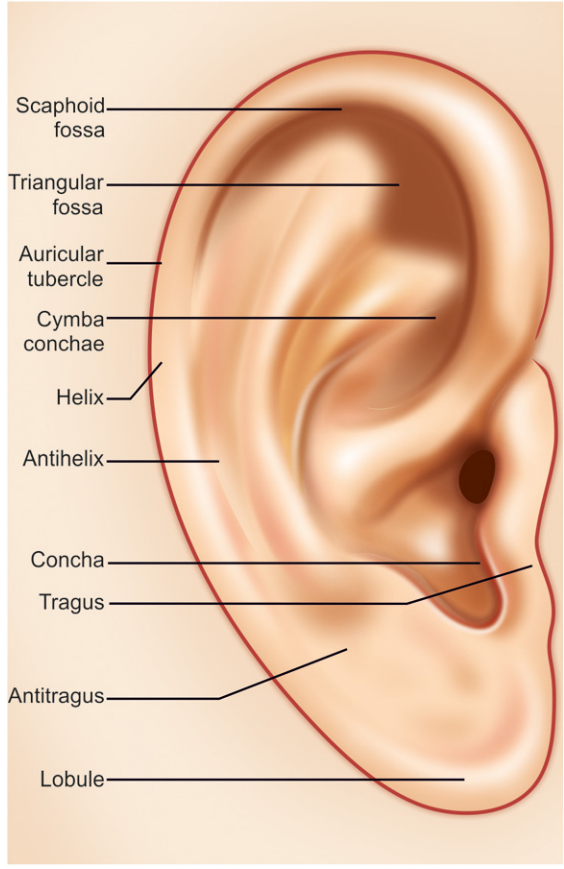


Fig. 51.1: Pinna: Anatomy

The nerve supply of the external ear is derived from the greater auricular nerve ($C_{2,3}$) lesser

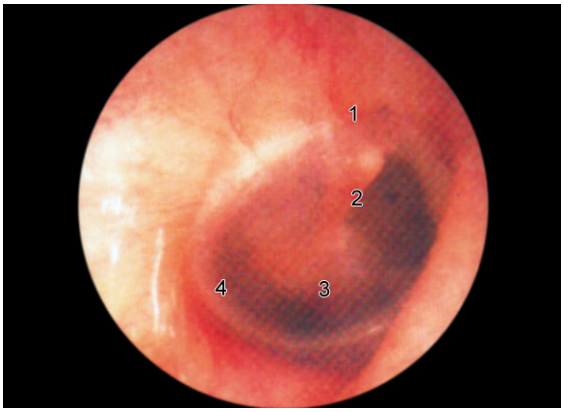


Fig. 51.2: Normal tympanic membrane

1. Pars flaccida
2. Handle of malleus
3. Pars tensa
4. Round window area

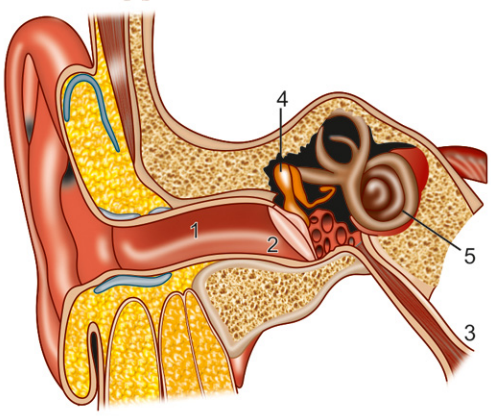


Fig. 51.3: Anatomy of ear—Right side

1. External auditory meatus
2. Tympanic membrane
3. Eustachian tube
4. Ossicles
5. Membranous labyrinth

occipital (C_2), auricular branch of vagus, auriculotemporal branch of mandibular division of the trigeminal nerve and a few fibers of the facial nerve. In a patient presenting with pain in the ear, if no local cause is detectable, distant sites supplied by these nerves should be examined. Referred otalgia is not uncommon. The nerve supply from facial nerve explains the appearance of herpetic vesicles in the external ear in herpes zoster affecting the geniculate ganglion of the facial nerve *(Ramsay-Hunt Syndrome)*

The *tympanic membrane* which forms the partition between the external auditory meatus and the middle ear is a pearly white glistening membrane with a cone of light in the anterior inferior quadrant. Functionally, it is a part of middle ear (Fig. 51.2).

The *middle ear* is an air filled cavity closely related to middle cranial fossa above and jugular bulb below. It communicates with the nasopharynx through eustachian tube anteriorly and to mastoid antrum and air cells posteriorly.

Infection from the nasopharynx can spread to middle ear through eustachian tube and from the middle ear it can spread to the mastoid antrum and air cells leading to mastoiditis, mastoid abscess and petrositis. Infection from the middle ear can spread upwards to the cranial cavity leading to extradural abscess, subdural abscess, brain abscess and meningitis which are potentially fatal, if undiagnosed.

The eustachian tube is wider, shorter and more horizontal in infants, thus permitting infection to travel from nasophanynx to middle ear readily. Milk may regurgitate into middle ear if the infants are not fed in head-up position. This may lead to acute otitis media.

During air travel, a person who has block in the eustachian tube can develop severe pain in the ear while landing. Since the eustachian tube is blocked, pressure in the middle ear and atmospheric pressure are not equalized as in the normals. Negative pressure develops in the middle ear and persists while landing leading to serous effusion.

Persons with block of the eustachian tube should be advised to inflate the middle ear forcibly by the Valsalva maneuver while landing. Blocking of the eustachian tube is common in persons with coryza and naso-respiratory allergy.

The normal appearance of the tympanic membrane is lost in diseases of middle ear. Tympanic membrane will have an oily appearance in serous otitis, and a bluish tinge in hemotympanum (bleeding). In retracted tympanic membrane, the cone of light is distorted with apparent fore shortening of handle of the malleus.

The middle ear contains three ossicles—malleus, incus and stapes; two muscles—the tensor tympani and stapedius, and the nerves corda tympani and the tympanic plexus. The tympanic plexus is formed by tympanic branch of the

glossopharyangeal nerve and sympathetic fibers from plexus around internal carotid artery.

The inner ear consists of bony and membranous labyrinths. The bony labyrinth consists of the three semicircular canals, the vestibule and the cochlea. The membranous labyrinth consists of the three semicircular ducts, utricle, saccule, cochlear duct, endolymphatic duct and sac.

The peripheral sense organ of hearing is the organ of Corti situated in the cochlear duct. The afferent impulses pass through the cochlear division of the eighth cranial nerve to reach the superior temporal gyrus which is cortical area of hearing.

The peripheral receptors of the vestibular system are the cristae located in the ampullae of semicircular ducts and the maculae of the utricle and saccule. The cristae of the semicircular canals respond to angular (rotatory) acceleration while those in the maculae of utricle and saccule respond to linear acceleration and gravity. Afferents from the peripheral receptors pass through the vestibular nerve to reach the vestibular nuclei from where efferents go to the nuclei of 3rd, 4th and 6th cranial nerves, the motor part of spinal cord, the autonomic nervous system and the temporal cortex.

Physiology of Hearing

Sound vibrations in the environment are directed to the external auditory canal by the pinna and the tympanic membrane vibrates. The vibrations are transmitted by the ossicular chain to the labyrinthine fluid which moves the basilar membrane.

The hair cells of the organ of Corti are stimulated and electrical impulses are produced which travel along the auditory nerve and pathway to reach the auditory cortex of the temporal lobe giving the sense of hearing. A normal person can hear frequencies of 20 to 20,000 hertz (Hz). Any defect in the pathway of sound conduction to inner ear or conduction of electrical impulses from inner ear to auditory cortex can result in different types of hearing loss.

Physiology of the Vestibular System

Body maintains its position and equilibrium by the use of three systems—the eye, the vestibular system and the central nervous system. In the central nervous system, we have the pyramidal system, the basal ganglia, cerebellum and proprioception system. Imbalance can result if there is pathology in any of these systems.

ANATOMY OF NOSE AND PARANASAL SINUSES

The external nose is pyramidal in shape and of a bony part constituted by nasal bones and frontal process of the maxilla and a cartilaginous part consisting of upper lateral cartilages, alar cartilage and sesamoid cartilages. The internal nose is divided into right and left nasal cavities by nasal septum. The nasal septum is formed by the perpendicular plate of the ethmoid, the vomer, the septal cartilage, the crest of the nasal bones, nasal spine of the frontal bones, rostrum of the sphenoid, crests of the palatine bones and the maxilla and the anterior nasal spine of the maxilla. Each nasal cavity has a lateral wall, medial wall, roof and floor. The lateral wall shows three projections, the inferior, middle and superior turbinates (conchae) and below and lateral to each turbinate is the corresponding meatus. The nasolachrymal duct opens into the anterior part of the inferior meatus. The frontal sinuses, the maxillary sinuses and anterior ethmoid cells open into the middle meatus. The posterior ethmoid sinus opens into the superior meatus (Figs 51.4 and 51.5).

The upper one-third of lateral walls up to superior turbinate, the corresponding part of nasal septum and roof of the nasal cavity form the olfactory region and the lower 2/3 of nasal cavity forms the respiratory region.

Smell is perceived in the olfactory region where the olfactory receptors are situated. The central processes of these receptors form the olfactory nerve

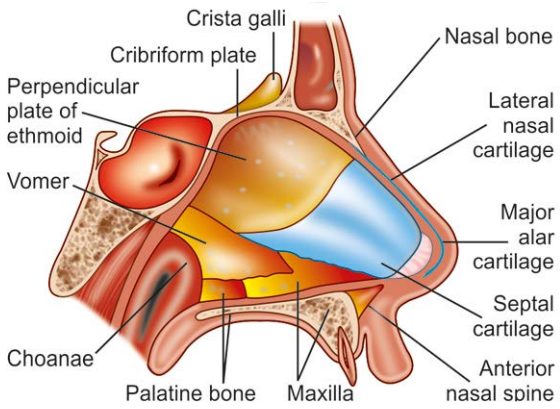


Fig. 51.4: Anatomy of nasal septum

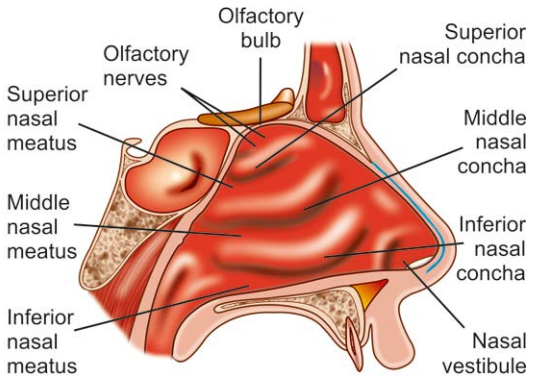


Fig. 51.5: Anatomy of lateral wall of nose

fibers which pass through the openings of the cribriform plate of ethmoid bone and synapse with cells of olfactory bulb and further fibers pass up to the pre-pyriform cortex and the amygdaloid nucleus.

Disorders of smell can occur if the odorous substance does not reach the olfactory area or if there is lesion in the olfactory mucosa or olfactory pathway. Ansomia (total loss of sense of smell) or hyposmia (partial loss of smell) can result from nasal obstruction from various causes including rhinitis. Injury to olfactory nerves or olfactory bulb in fractures of anterior cranial fossa and intracranial lesions like abscesses, tumors or meningitis which cause pressure on olfactory—tracts lead to ansomia or other disorders of smell. Parosmia (perversion of smell) is seen in the recovery phase of post influenzal anosmia and intracranial tumors.

The blood supply of nose is from several arteries which are branches of the external carotid artery. The anterior inferior part of the septum is very vascular and is called. *"Little's area"* where four arteries anastamose to form the *Kiesalbach's plexus.* This area is a common site for epistaxis. Cauterization of veins in this region is resorted to at times, to arrest bleeding.

The *paranasal sinuses*—the maxillary, frontal, ethmoid and sphenoid—are air filled cavities which open into the nose. Probable functions of the paranasal sinuses are:

1. Air conditioning of inspired air
2. Resonance of voice
3. To act as thermal insulators of eyeballs and brain
4. To reduce the weight of the skull.

The anterior part of nasal cavity is called vestibule and is covered by skin containing sebaceous glands and hair follicles and hence furuncles may occur in this part.

ANATOMY OF PHARYNX

Pharynx is a fibromuscular tube forming the upper part of air and food passages. It is divided into nasopharynx, oropharynx and laryngopharynx. The nasopharynx extends from base of skull to the horizontal plane passing through the hard palate. A collection of lymphoid tissue at the junction of the roof and posterior wall of nasopharynx is called adenoid. Pathological enlargement of the adenoid in children may produce nasal obstruction, mouth breathing and snoring. This may necessitate adenoid curettage. Eustachian tube opening is situated in the lateral wall of nasopharynx and just behind the opening is the *fossa of Rosenmuller* which is a common site for malignancy. Examination has been made easy with the availability of rigid and flexible endoscopes (Fig. 51.6).

The oropharynx extends from the plane of hard palate above to the level of hyoid bone below. The tonsils are present on the lateral wall. Sometimes in children the tonsils are enlarged leading to obstruction to breathing. Tonsillectomy used to be a very common surgical procedure till recent times.

Hypopharynx or laryngopharynx extends from the level of hyoid bone to the lower border of cricoid cartilage. Clinically it is divided into three regions – the pyriform sinus, the post-cricoid region

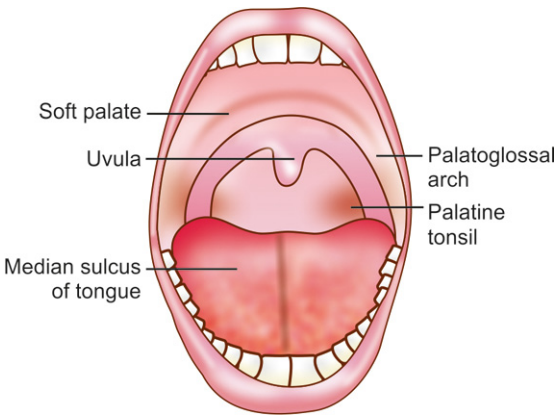


Fig. 51.6: Anatomy of oropharynx

and posterior pharyngeal wall. The post-cricoid region is a common site for carcinoma in females suffering from Plummer Vinson syndrome.

ANATOMY OF LARYNX

Larynx is an integral part of the respiratory tract and it contains the vocal cords which are the main organs for voice production. The length of vocal cords antero-posteriorly is 24 mm in adult males and 16 mm in adult females. Larynx is made up of cartilages, muscles, ligaments and joints. It lies in front of the laryngopharynx opposite the third to sixth cervical vertebrae. Voice is produced by vibrations of the vocal cords when air under pressure from the sub-glottic area passes through the vocal aperture. This voice is converted into speech by the modulatory actions of lips, tongue, palate, pharynx and teeth. The muscles which act on the vocal cords are posterior cricoarytenoid (abductors), lateral cricoarytenoid and inter-arytenoids (adductors) and cricothyroid and thyro-arytenoid (tensors of vocal cords). All these muscles except the cricothyroid are supplied by the recurrent laryngeal nerve. The cricothyroid muscles are supplied by external laryngeal nerve. Sensory supply above the vocal cords is by internal laryngeal nerve and below the vocal cords by recurrent laryngeal nerve. During quiet respiration, the distance between the two vocal cords is about 14 mm and in deep respiration it can widen up to 19 mm (Fig. 51.7).

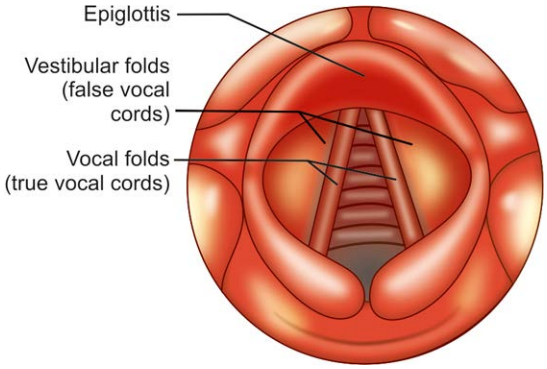


Fig. 51.7: Larynx anatomy

The larynx of an infant differs from that of an adult in being small, funnel shaped and of a narrower lumen. Cartilages are also softer and they collapse easily. In addition, there is more of submucosal tissue which makes it more liable to become edematous in response to trauma, allergy and inflammation.

At puberty, the larynx of males grow rapidly with increase in length of rima glottidis and change in character of the voice. The larynx of females does not undergo such major changes. *Pubophonia* is the term used to denote the persistence of high pitched voice in males without undergoing pubertal change.

CHAPTER

52 Clinical Examination in ENT Diseases

OS Radhakrishna Pillai

Symptoms in diseases of the ear, Common symptoms in diseases of nose, paranasal sinuses and nasopharynx, Symptoms in diseases of oral cavity and oropharynx, Symptoms in diseases of laryx and laryngopharynx, Physical examination, ENT examination

SYMPTOMS IN DISEASES OF THE EAR

Pain in the Ear: Otalgia

In *furuncles and otitis externa*, there is aggravation of pain on opening of the mouth and chewing. There is tenderness on pressure over the tragus and on pulling the pinna. In *acute otitis media* and *acute exacerbation of chronic otitis media*, ear discharge and hearing loss are present. *Myringitis bullosa* is characterized by vesicles over the surface of the tympanic membrane which may burst, producing blood stained discharge. Malignant growths of external and middle ear may present as growths in the ear giving rise to blood stained discharge and deafness.

Ear lesions may cause referred pain which may be felt as headache, even before local pain is manifest.

Diseases from distant sites may cause pain referred to the ear. The pain may be referred along the trigeminal, facial, glossopharyngeal, vagus, greater auricular and lesser occipital nerves. Some important causes of referred otalgia ear are given in Table 52.1.

Table 52.1: Common causes of otalgia

1. Furuncle ear
2. Diffuse otitis externa
3. Myringitis bullosa
4. Herpes Zoster
5. Keratosis obturans
6. Acute otitis media
7. Malignant otitis externa
8. Malignant growths of external and middle ear

a. *Via trigeminal nerve:* Impacted wisdom tooth, caries teeth, dental abscess, ulcers and malignant growths of anterior 2/3 of tongue and floor of mouth, temporomandibular arthritis and malignancy of nose, paranasal sinuses or nasopharynx.
b. *Via facial nerve:* Geniculate ganglion herpes.
c. *Via glossopharyngeal nerve:* Acute tonsillitis, peritonsillar abscess and malignancies of tonsil, base of tongue and oropharynx.
d. *Via vagus nerve:* Malignancy of larynx and laryngopharynx.
e. *Via greater auricular and lesser occipital nerves:* Cervical spine lesions, inflammatory and traumatic lesions of neck.

It is important to examine these sites in all cases of otalgia when a local cause cannot be detected.

Discharge From the Ear (Table 52.2)

The character of ear discharge, its amount and odor are to be noted. Watery discharge is usually seen in otitis externa. In chronic suppurative otitis media of tubotympanic type, the discharge is mucoid or mucopurulent, not foul smelling and occurring continuously or intermittently. During attacks of

Table 52.2: Common causes of discharge from ear

1. Acute and chronic otitis media
2. Otitis externa—acute and chronic
3. Eczematous dermatitis of external ear
4. Myringitis bullosa
5. Otomycosis
6. CSF otorrhea

upper respiratory infection the discharge becomes profuse. In atticoantral diseases the discharge is usually scanty but very foul smelling. Blood stained discharge is seen in myringitis bullosa, chronic suppurative otitis media with granulations, malignancy of middle ear and rarely glomus jugulare tumor. Cerebrospinal fluid (CSF) otorrhea appears as a clear watery discharge. This is usually due to fracture or erosion of the base of the skull.

Deafness

Even though the term deafness should better be reserved for total loss of auditory function and the term hearing loss used for partial hypoacusis, in clinical practice "deafness" is used to denote impairment of hearing. For purposes of compensation and other legal purposes the term 'deaf' is used to denote those in whom the sense of hearing is nonfunctional for day-to-day life. In day-to-day life usually hearing loss of over 70 dB (decibels) in speech frequencies will be considered nonfunctional.

Hearing impairment may be unilateral or bilateral. A detailed history should include the onset, duration, progress, presence of predisposing factors and presence of deafness in family members (Tables 52.3 to 52.6).

Table 52.3: Common causes of conductive hearing loss

1. Congenital	Atresia of external auditory canal, stenosis of external auditory canal, anomalies of middle ear ossicles
2. Traumatic	Perforation of tympanic membrane ossicular, discontinuity, hemotympanum
3. Inflammatory	Acute and chronic otitis media, serous effusion into middle ear
4. Neoplastic	Benign and malignant growths of external auditory canal and middle ear
5. Miscellaneous	Wax and foreign bodies in ear, otosclerosis, tympanosclerosis, adhesive otitis

Table 52.4: Common causes of sensorineural hearing loss in neonates

1. Genetic factors
2. Maternal infections—toxoplasmosis, rubella, cytomegalovirus infection, herpes, syphilis
3. Drugs during pregnancy
4. Diseases of mother—diabetes, hypothyroidism, toxemia of pregnancy
5. Prematurity—birth injury
6. Neonatal jaundice
7. Neonatal meningitis

Table 52.5: Common causes of sensorineural hearing loss in children

1. Genetic factors
2. Traumatic—fracture temporal bone
3. Infections—measles, mumps, varicella, influenza, meningitis, encephalitis
4. Ototoxic drugs—e.g. streptomycin
5. Noise induced—exposure to very loud sounds or explosive blasts

Table 52.6: Common causes of sensorineural hearing loss in adults

1. Infections—labyrinthitis—bacterial, viral, spirochetal
2. Trauma to inner ear or auditory nerve from fracture of temporal bone
3. Ototoxic drugs—neomycin, kanamycin, streptomycin, diuretics, salicylates, quinine, chloroquine, cytotoxic drugs
4. Noise induced deafness, e.g.—aircraft sounds, fireworks
5. Presbyacuisia—i.e. hearing less acutely due to old age
6. Meniere's disease
7. Acoustic neuroma
8. Systemic diseases—diabetes—hypothyroidism, chronic renal diseases, autoimmune diseases, blood diseases, multiple sclerosis

Types of Deafness

Conductive deafness is due to a defect in the sound conducing mechanism of the ear. *Sensorineural deafness* is due to lesion in the cochlea, auditory nerves and central connections.

Psychogenic Deafness

a. Malingering where there is a conscious effort on the part of the person to deceive
b. Hysterical, where there is a subconscious wish to raise the hearing threshold and hence, outside the patient's control.

Deafness of sudden outset may follow head injury, blast injury, viral infections or vascular accidents of the brain. A detailed history, full clinical examination and various hearing tests are required to diagnose the type and degree of hearing loss and plan treatment.

Tinnitus

Tinnitus indicates hearing of adventitious sounds. It is said to be subjective when audible only to the patient and objective when audible to others also. Objective tinnitus may be due to myoclonus involving the palatal muscles, tensor tympani or stapedius muscle, arteriovenous shunts, glomus jugulare tumors, and aneurysms of occipital artery, superficial temporal artery and aortic arch. Subjective tinnitus may be due to various causes like wax in the ear, sensorineural deafness of different etiology, otosclerosis, acoustic trauma,

anemia, leukemia, hypertension and renal diseases. Emotional factors may also cause tinnitus and in turn, tinnitus itself may lead to anxiety. There is still another group in whom no cause is detectable (idiopathic tinnitus).

Vertigo

Vertigo is defined as a sensation of rotation or unsteadiness which the patient may experience. The history goes a long way in the diagnosis of its etiology. It is important to ascertain whether the patient's complaint is a true sensation of rotation or a syncopal attack in which patient gets a blackout, falls momentarily, and quickly regains conciousness (Table 52.7).

Other symptoms of neurosis like palpitation, breathlessness, fatigue, insomnia, sweating and tremors may be present. In these patients there will no nystagmus or hearing loss.

Episodic vertigo with fluctuating deafness and tinnitus is characteristic of *Meniere's disease*. Upper respiratory cattarrh followed by vertigo should suggest viral labyrinthitis or vestibular neuronitis. Benign positional vertigo is characterized by vertigo at certain positions of head and may be seen in chronic suppurative otitis media and in head injury. Patients taking ototoxic drugs may also get vertigo. Vertigo with discharging ear may be due to labyrinthitis.

Table 52.7: Common causes of vertigo

Peripheral vestibular disorders
1. Labyrinthitis 2. Benign paroxysmal positional vertigo 3. Meniere's disease 4. Vestibular neuronitis 5. Acoustic neuroma 6. Perilymph fistula 7. Vestibulotoxic drugs 8. Head injury and acoustic trauma
Central vestibular disorders
1. Cerebovascular accidents 2. Vertebrobasilar insufficiency 3. Cerebellar disease 4. Multiple sclerosis 5. Tumors of brain stem and fourth ventricle 6. Cervical vertigo
Ocular causes
1. Refractive errors 2. Intraocular muscle paralysis 3. Refractive errors and intraocular muscle paralysis can result in vertigo
Psychogenic vertigo
1. Psychogenic vertigo results from tension and anxiety

COMMON SYMPTOMS IN DISEASES OF NOSE, PARANASAL SINUSES AND NASOPHARYNX

Nasal Obstruction

This may be unilateral or bilateral, continuous or intermittent. In infants nasal obstruction may be due to congenital atresia, adenoids, allergic rhinitis, secretions, or obstructing foreign bodies. In children nasal obstruction may be due to adenoids, foreign bodies in the nose, rhinoliths, nasopharyngeal fibroma, antrochoanal polyp and injury to nose leading to fracture of nasal bones.

In adults nasal obstruction may be due to deviated nasal septum, nasal allergy, polyps, rhinosporidiosis and benign or malignant growths in the nose and paranasal sinuses.

Nasal Discharge

Thin watery discharge is commonly seen in coryza. The discharge is mucopurulent or purulent in infection of the nose and paranasal sinuses. Foul smelling discharge with crusts falling out from the nose is seen in atrophic rhinitis. Blood stained discharge is seen in rhinosporidiosis, angiofibromas, malignancies of nose and paranasal sinuses and granulomatous diseases.

Unilateral nasal discharge in children is usually due to foreign body or nasal diphtheria. Clear watery discharge from the nose on stooping suggests CSF rhinorrhea.

Headache

This is a very common symptom in ENT diseases. The site of headache, the time of onset and duration, its periodicity, and any radiation should all be asked for. Headache due to frontal sinusitis is localized to forehead, starts in early hours of the day and subsides in the afternoon, since by this time, the pus is discharged from the sinus. Maxillary sinus headache is felt over the maxillary sinus region and may be referred to the lateral aspects of the forehead and upper alveolus. Pain in ethmoidal sinusitis is localized to the medial canthus. Sphenoid sinus

headache is usually felt over the vertex, occiput or behind the eyes.

Epistaxis

Bleeding from nose is called epistaxis. It may be due to local or general causes. Infection of nose and paranasal sinuses, congenital telangiectasis involving nasal septum, trauma to nasal mucosa, growths in the nose, paranasal sinuses and nasopharynx, presence of foreign bodies and rhinosporidiosis are common local causes of epistaxis. In children, repeated bleeding may occur from the prominent retrocolumellar vein. Recurrent, profuse, painless bleeding from nose in children is characteristic of nasopharyngeal angiofibroma.

In adults atherosclerotic changes in the vessels of nose and hypertension are common causes of nasal bleeding. Epistaxis is a common prodromal symptom in several infections such as rheumatic fever and influenza. Purpuric disorders may cause epistaxis as one of the hemorrhagic manifestations.

Anosmia

Loss of sense of smell may occur as a result of destructive lesions of nose, lesions affecting the olfactory nerves, fracture of the anterior cranial fossa and central lesions of brain involving uncus and hippocampus. Anosmia may be uni- or bilateral. Bilateral anosmia is a frequent symptom in hysteria.

Sneezing

This is a reflex reaction initiated by abnormal stimulation of nasal mucosa. This is a common symptom of nasal allergy, foreign bodies in the nose, and rhinitis. The reflex is similar to cough reflex with the following differences. The area of stimulation is the nasal mucosa. The air is ejected forcibly through the nose so as to blowout discharges or other irritants from the nostrils.

Nasal Voice

Diseases of nose and nasopharynx produce change in tone of voice. Enlarged adenoids and nasopharyngeal tumors cause closed nasal voice called *rhinolalia clausa*. Palatal paralysis, cleft palate and short palate lead to hypernasality of voice called rhinolalia aperta.

SYMPTOMS IN DISEASES OF ORAL CAVITY AND OROPHARYNX

Pain in the throat: This is a very common symptom which occurs in acute infections of oral cavity and oropharynx. Ulcers of mouth or oropharynx, tonsillitis and malignancy are the other common causes.

Dysphagia: Difficulty in swallowing is called dysphagia. This may be due to a variety of lesions in the oral cavity, pharynx or esophagus. The lesion may be inflammatory, paralytic or neo-plastic.

Odynophagia: Pain on deglutition may be due to inflammatory lesions in the oropharynx, laryngopharynx or esophagus. Malignancy of the oropharynx or laryngopharynx can also cause odynophagia Impaction of fish bone in the throat is a notuncommon cause of odynophagia in India.

Irritant cough: Diseases which produce irritation of throat due to inflammation, allergy or presence of secretions can lead to irritant cough. Regurgitation of acid gastric contents into the esophagus is a common cause of irritant cough (gastroesophageal reflux disease—GERD)

SYMPTOMS IN DISEASES OF LARYNX AND LARYNGOPHARYNX

Hoarseness of voice: Even though the term hoarseness literally means a rough and harsh sound, it is generally used to denote a change in the character of voice, as the patient may just complain of an altered voice and may not be able to describe accurately the type of change in the voice. Any disease which interferes with the movement and vibration of vocal cords can produce hoarseness of voice. Acute and chronic laryngitis, laryngeal paralysis, congenital lesions, chronic granulomatous lesions and benign and malignant tumors are the common causes of hoarseness of voice.

Complete loss of voice is called *aphonia*. Functional aphonia may occur in hysterical patients and can be diagnosed by the fact that the patient can cough effectively and the vocal cords will be seen to move on laryngoscopic examination.

Dysphonia: It is abnormal alteration of vocal sounds.

Phonaesthenia: Weakness of the voice due to weakness of muscles of phonation is called

phonaesthenia. This is sometimes seen in professionals who use their voice continuously and for prolonged periods irregularly.

Pubophonia: It is the change in voice that starts around puberty in males and is characterized by cracking or break in voice.

Pain: Pain lower down in throat is usually seen in perichondritis, tuberculosis or carcinoma of larynx. The pain may be referred to the ear also.

Irritant cough: Dry cough may be due to irritation in the vocal cords by secretions or due to foreign bodies, polyps, granulations, and benign and malignant growths of the larynx.

Dyspnea: Any disease which produces laryngeal obstruction may result in dyspnea. Edema of the larynx, foreign bodies in the larynx, juvenile multiple papillomatosis and carcinoma are some of the laryngeal causes of dyspnea. These lead to stridor which is harsh sound heard during respiration.

Laryngeal stridor: The term is used to denote a peculiar noisy inspiration associated with dyspnea caused by laryngeal obstruction. The inspiration becomes noisy when air is sucked in through the obstruction. During expiration wheeze may be heard. Congenital laryngeal stridor, laryngismus stridulus occurring in tetany, foreign bodies in the larynx, acute laryngo-tracheobronchitis, laryngeal diphtheria, cysts of larynx and benign and malignant tumors of larynx are some of the common causes of laryngeal stridor.

Dysphagia: This is a common symptom in diseases of laryngopharynx. Carcinoma of pyriform fossa, postcricoid region and posterior wall of laryngopharynx lead to progressive dysphagia. Painful swallowing or odynophagia may be the only symptom in tuberculosis of larynx at times.

Feeling of lump in the throat: It is usually complained of by patients with supraglottic malignancy, especially when involving the aryepiglottic folds. This is a common symptom in iron deficiency states and hysterical subjects (globus hystericus).

General Scheme of Examination

The process of eliciting the history and physical examination follows the same principles described for all diseases in general. The procedure for conducting ENT examination is listed below.

The examination is preferably performed in:

1. Detailed history
2. General examination
3. Local examination
4. Systemic examination when required
5. Investigations.

With this routine, the diagnosis can be obtained in almost all cases.

PHYSICAL EXAMINATION

General appearance of the patient may give diagnostic clues in many cases. A child with adenoids may have the typical "adenoid facies", consisting of open mouth, vacant expression, underslung jaw, protuberent anterior teeth, malar prominence and pinched nose. Nasopharyngeal fibroma may lead to "frog faced deformity" with widening of the root of nose, proptosis and lateral shift of eyes. In peritonsillar abscess the head is turned towards one side with saliva dribbling from the angle of the mouth.

SYSTEMIC EXAMINATION

General systemic diseases may present with ENT manifestations. For example, epistaxis may be caused by hypertension, acute leukemia or purpura. Left vocal cord paralysis may be due to pressure on the left recurrent laryngeal nerve occurring in bronchogenic carcinoma and mitral stenosis, Right vocal cord paralysis may follow right apical tuberculosis. Pulmonary tuberculosis may present as hoarseness of voice caused by tuberculous ulceration of the larynx. Sinusitis may be a manifestation of *Kartagener's syndrome* which consists of dextrocardia, *situs inversus*, bronchiectasis and sinusitis. Similarly ENT diseases may lead to systemic complications. Infection of the ear, mastoids and paranasal sinuses may spread intracranially to form intracranial abscess or meningitis. Pus from the sinuses may be aspirated into the bronchi and lungs to produce bronchitis and pneumonia. A furuncle of the nose may lead to cavernous sinus thrombosis. Malignancies of larynx and maxillary antrum may produce secondary deposits in bones, liver and lungs. Nasopharyngeal carcinomas may infiltrate the base of the skull leading to paralysis of the lower cranial nerves.

Special Points to be Taken Care are Given Below

History

Some diseases may have direct relationship with occupation of the patient and this has to be enquired into. For example, deafness may develop in persons working in nosiy surroundings and hoarseness of voice is a common symptom in professionals who strain their voice. After recording the presenting complaints, their evolution and past treatment if any, have to be noted.

Positive interrogation may be required to bring out associated symptoms which the patient may not volunteer. For example, in a case with vertigo as the major complaint, the occurrence of deafness or discharge from the ear may not be forthcoming, unless leading questions are asked.

Care should be taken to elicit past illnesses such as syphilis, typhoid, mumps, and tuberculosis which may produce sensorineural deafness or recurrent tonsillitis which may be the source for infection of the middle ear and mastoids. The family history may give clues to diagnose diseases such as otosclerosis, Pendred's syndrome, hemophilia, multiple telangiectasis, acoustic neuromas and several others which run in families.

Heavy smoking, alcoholism and the habit of chewing tobacco with betel, areca nut and lime are factors which predispose to malignancies in the mouth, pharynx, and larynx.

Local Examination of ENT Organs

The organ to be examined first will depend upon the main complaint. But since ear, nose, nasopharynx, oropharynx and larynx are inter-related, examination is complete only when all these regions are totally examined. The method of examination of each region is described separately.

Minimum Instruments Required

1. One set of ear speculum, preferably black finish
2. One set of *Thudichurn' s nasal speculum* with different sizes of nasal blades
3. *Lack's tongue depressor*
4. Laryngeal mirror of different sizes (sizes 3 are more commonly used)
5. Postnasal mirror of different sizes (sizes 0,1 and 2 are used more frequently
6. Siegle's pneumatic speculum
7. Tuning forks of frequencies 256, 512 and 1024 Hz
8. Jobson-Hom probe.

EQUIPMENT REQUIRED FOR PERFORMING PROPER PHYSICAL EXAMINATION

These include an ENT examination chair and illumination by a Bull's eye lamp and head mirror or the Clar head light (Figs 52.1 to 52.3). Fiberoptic head lights and the revolving head light source provided with ENT treatment units are more modern sophisticated equipments.

The examination is preferably performed in a semidark room. The patient should be seated in front of the examiner on an ENT examination chair, leaning forward slightly with his back kept straight and feet on the floor. The examiner sits in front of the patient on a revolving chair. If the Bull's eye



Fig. 52.1: Set up for ENT examination



Fig. 52.2: Correct method of using the head mirror

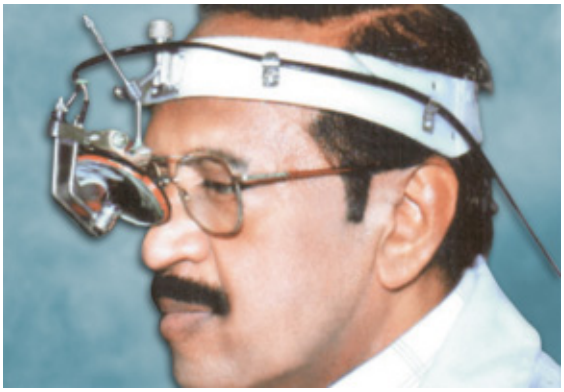


Fig. 52.3: Clar headlight in use



Fig. 52.4: Method of holding a child for ENT examination

lamp and head mirror are used, the light source is kept above and behind the left shoulder of the patient at the level of his left ear. The head mirror which is a concave mirror 10 cm in diameter with a focal length of about 20 cm is worn by the examiner and manipulated to focus the light on the part to be examined (Fig. 52.2). The right eye of the examiner sees through the hole of the mirror while the left eye sees directly.

The examination of children requires special mention. The child is seated on the lap of the parent with his legs held firmly between her legs (Fig. 52.4). Left hand of the parent holds the child's hands in front of his chest while his right hand holds the child's forehead to fix the head. If possible, children are examined without using instruments.

EXAMINATION OF THE EAR

Inspection

Pinna

Patient's head is turned to one side so that the ear to be examined is towards the examiner and the light is reflected on to that ear (Figs 52.5 to 52.8). Any obvious pathology in the pinna is noted. Congenital anomalies like microtia, macrotia, anotia and bat ear are easy to diagnose. Swelling of the pinna occurs in hematomas, perichondritis or abscess. Allergic oedema of pinna is usually due to medicaments like chloramphenicol ear drops or due to wearing of new ornaments. Erysipelas of face may extend to pinna. Ulcers of pinna may be benign or malignant. Rodent ulcer, squamous cell carcinoma, ulcerated molluscum sebaceum and eczematous dermatitis are some of the common ulcerating lesions. Congenital pre-auricular sinus is seen as a discharging opening at the root of the helix.

Preauricular Region

This should be inspected. Swelling in this region is usually caused by preauricular lymphadenitis or ulceration of infected preauricular sinus.

Postauricular Area

This should also be inspected carefully for swelling, scar, sinus or fistula. Swelling in the postaural area may suggest sub-periosteal abscess, postauricular lymphadenitis,cellulitis spreading from furuncle of external ear canal, allergic dermatitis or benign tumors. *Postauricular edema at site of emergence of mastoid emissary vein suggests thrombosis of the sigmoid sinus. This sign is called Greisinger's sign.* Inspection of postaural sulcus gives clue to the cause of the swelling. The sulcus is not obliterated in mastoid abscess whereas in postauricular edema due to furuncle in the ear the sulcus is obliterated.

External Auditory Canal

In adults the external auditory canal of the right ear is brought into view by pulling the pinna upwards and backwards with the thumb and index finger of the left hand (Fig. 52.5). For the left ear the right hand is used.

The method brings the outer cartilagenous part in line with the inner bony part and allows full view of the external auditory canal and tympanic membrane. While pulling on the pinna, the facial expression of the patient should be watched. In acute inflammatory diseases of the cartilaginous part of



Fig. 52.5: Inspection of right auditory canal



Fig. 52.7: Method of using ear speculum for right ear



Fig. 52.6: Method of syringing the ear for removal of wax and foreign body



Fig. 52.8: Method of using ear speculum for left ear

external canal, the patient complains of pain which may be severe so that she may jump out of the seat. In children, the pinna should be pulled downwards and backwards to visualize the external auditory canal because the external auditory canal is more horizontal in them. Congenital atresia or narrowing can be easily made out. Wax, fungal growth, foreign bodies, polyps and tumors in ear canal should be looked for. If there is discharge, its nature should be noted. The ear should be cleaned by dry mopping with a sterile cotton swab or by gentle suction to facilitate further examination. Wax should be removed by wax hook or by syringing of the ear. Fungal growth can also be cleaned by sterile cotton. Foreign bodies are best removed by syringing (Fig. 52.6). In cases where there are polyps or growths in the external auditory canal, they can be differentiated by gentle probing (Figs 52.7 and 52.8).

Tympanic Membrane

An ear speculum of appropriate size is gently introduced with a rotating movement up to the cartilaginous part of the external auditory canal to bring the deeper bony part of the canal and tympanic membrane into view. The speculum is introduced with right hand and then held with the thumb and index finger of left hand, while the middle and ring fingers of the left hand pull the pinna upwards, and backwards (Figs 52.7 to 52.9).

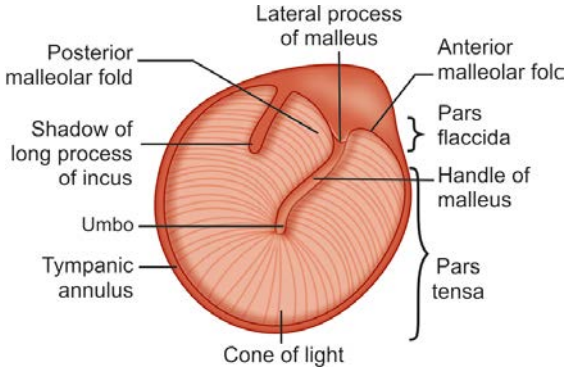


Fig. 52.9: Normal tympanic membrane—anatomy

This brings the tympanic membrane clearly into view.

Normal tympanic membrane is a thin lustrous pearly grey translucent membrane set obliquely between the external auditory canal and middle ear. It is oval in shape, concave, and measures approximately 10 mm vertically and 8 mm horizontally. Maximum concavity is in the center and it is called umbo. An ivory colored ridge is seen running upwards and forwards from the umbo. It is produced by the handle of the malleus which ends above in a tiny knob of pin head size the short process of the malleus. The anterior and posterior malleolar folds run anteriorly and posteriorly from the handle of malleus dividing the lympanic membrane into two parts. The upper part is pars flaccida (Shrapnell's membrane) and the lower part is pars tensa. The cone of light is a conical reflection of light which extends in the anteroinferior quadrant of the ear drum. The pars tensa is divided into four quadrants by an imaginary line extending downwards from the handle of malleus and another at right angle to it at the level of the umbo. These are anterosuperior, anteroinferior, posterosuperior and posteroinferior quandrants (Fig. 52.9).

In infants the tympanic membrane is thicker and more horizontally placed so that the cone of light and lustre of tympanic membrane, may not be seen.

Any pathology of the tympanic membrane should be carefully noted. If there is a perforation of the tympanic membrane, the site and size of the perforation, the color of the middle ear mucosa seen through the perforation and other lesions in the middle ear as seen through the perforation are to be noted.

Types of Tympanic Membrane Perforation (Figs 52.10A to E)

1. *Central perforation:* Perforation is in pars tensa with a rim of tympanic membrane all around it.
2. *Marginal perforation:* The perforation is in pars tensa and part of the circumference of the perforation is formed by the bony wall.
3. *Attic perforation:* The perforation is situated in pars flaccida.
4. *Subtotal perforation:* It is very large central perforation.
5. *Total perforation:* It is one when the whole of the pars tensa with the tympanic annulus is involved.

Attic and marginal perforations are usually seen with atticoantral type of chronic suppurative otitis media.

In acute otitis media, the tympanic membrane may be red, congested and bulging. Vesicles on tympanic membrane are seen in myringitis bullosa. Lustreless tympanic membrane with an oily appearance is seen in secretory otitis media. Tympanic membrane is blue in hemotympanum and in cholesterol granuloma. The tympanic membrane shows a flamingo pink appearance in active otosclerosis called *Schwartze sign.* A white patch over the tympanic membrane is seen in tympanosclerosis. Cholesteatoma of middle ear is usually

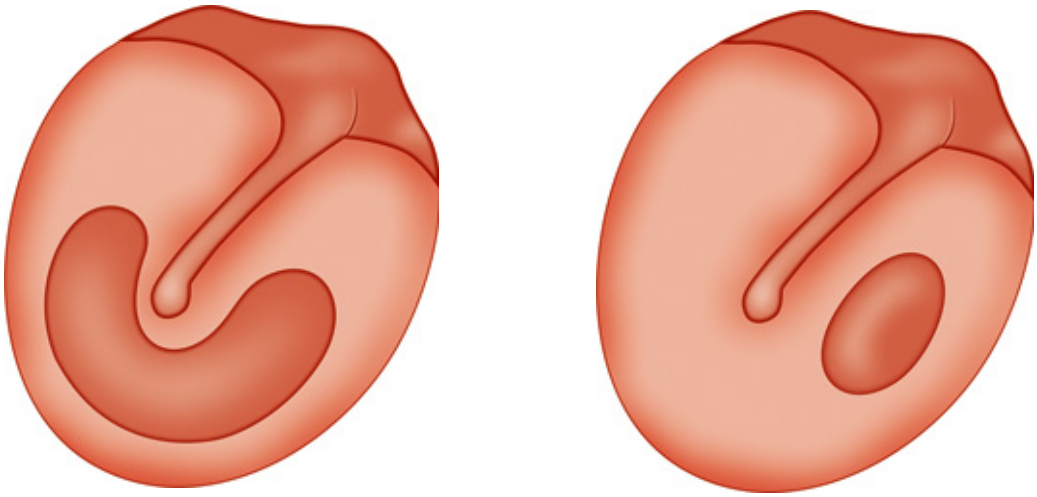


Fig. 52.10A: Central perforation

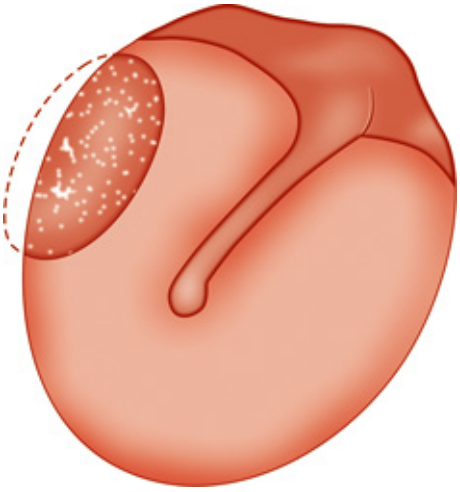


Fig. 52.10B: Marginal perforation

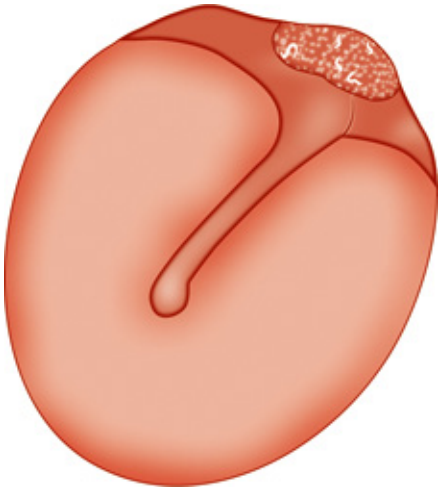


Fig. 52.10C: Attic perforation

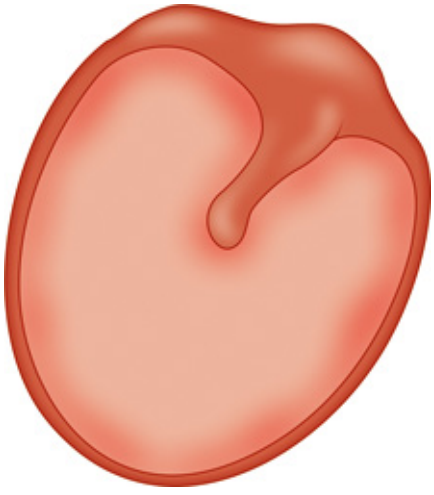


Fig. 52.10D: Subtotal perforation

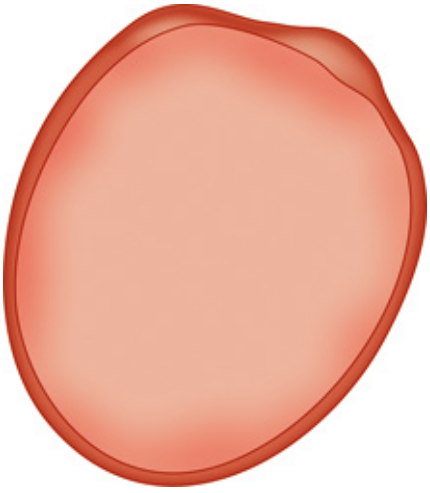


Fig. 52.10E: Total perforation

seen as white flakes with a characteristic foul smell. Retraction of the tympanic membrane may be evidenced by the following features:

1. Distortion of cone of light
2. Apparent shortening of the handle of malleus
3. Prominence of lateral process of malleus and anterior and posterior malleolar folds. When the tympanic membrane is retracted, the patency of the eustachian tube and mobility of the tympanic membrane are to be tested by Valsalva's maneuver and with the use of Siegle's pneumatic speculum. Valsalva maneuver is performed by asking the patient to blow his cheeks and inflate the ears with the nose and mouth closed, while the surgeon views the tympanic membrane. A definite outward movement of posterior half of pars tensa indicates that the eustachian tube is patent and tympanic membrane is mobile.

Examination Using Siegle's Pneumatic Speculum (Figs 52.11 and 52.12)

Siegle's pneumatic speculum is an aural speculum which gives a magnification of 2.5 and which is provided with a rubber bulb for increasing or decreasing the pressures in the external auditory canal. Using a speculum of the proper size tympanic membrane is visualized and the patient is asked to do the Valsalva's maneuver. The tympanic membrane is observed to bulge. The pressure in the external auditory canal can be altered by compression or release of the rubber bulb and the mobility of the membrane is also studied. The use



Fig. 52.11: Examination using Siegle's pneumatic speculum right ear



Fig. 52.12: Examination using Siegle's pneumatic speculum left ear

of Siegle's pneumatic speculum helps to detect mobility of the tympanic membrane, patency of eustachian tube, pin hole perforation of the membrane, to differentiate an open perforation from a thin healed perforation and to elicit the fistula sign.

In case where the tympanic membrane looks absolutely normal, further examinations like hearing tests and vestibulbar function tests are carried out depending on the patient's complaints.

Palpation

Preauricular and postauricular regions should be palpated.

Mastoiditis is characterized by tenderness over mastoid antrum, which can be elicited by gentle pressure over the cymba concha.

Auditory Function Tests

1. Conversational and whispering voice test
2. Tuning fork tests
3. Audiometry.
 - I. Subjective audiometry—Pure tone audiometry, Speech tone audiometry, Bekesy self recording audiometry.
 - II. Objective audiometry—Impedance audiometry, psychogalvanic skin resistance audiometry, evoked responses audiometry, electrocochleography.

Voice test and tuning fork tests are performed along with the clinical examination. The others are done as special investigations.

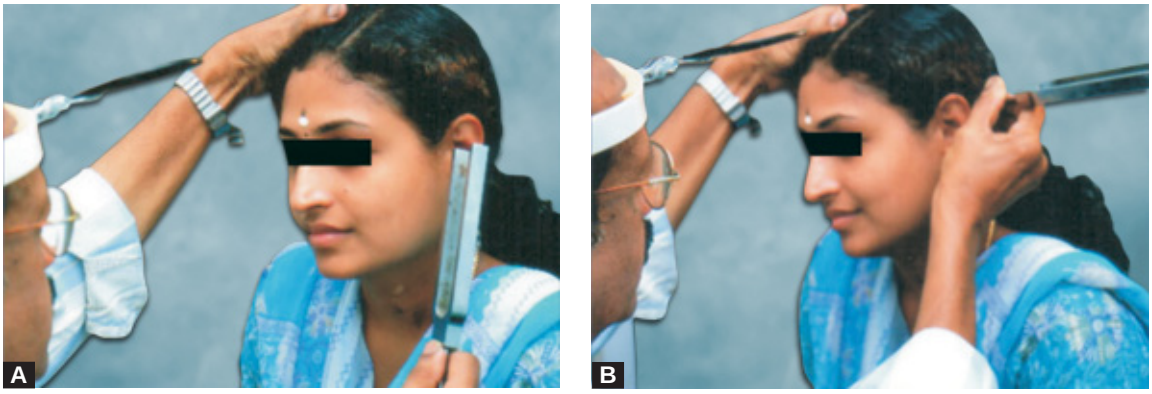
Conversational and Whispering Voice Test

In these tests, the examiner measures the distance at which the patient can hear and repeat conversation and whispered speech. A normal person will be able to hear speech at conversational level at 12 meters and whispered voice at 6 meters in a very quiet room. Since most of the rooms in which hearing tests are carried out do not allow a distance greater than 6 meters, it has become customary to consider 6 meters as the distance for normal standard. The patient is first instructed to repeat what the examiner says without watching the examiner's lips. Normal conversational voice is used first and then whisper voice. Both ears are tested separately. The ear not being tested is masked by a finger inserted into the external auditory canal or by producing some sound in that ear (e.g. repeatedly pressing the tragus over the external canal or rubbing a piece of paper over the pinna or by using a Barany's noise box).

The distance at which the patient repeats the conversation and whispered voice is noted, the test is repeated on the other side also. This test helps to compare the hearing in both ears and also to get a preliminary idea about gross hearing defects.

Tuning Fork Tests

These tests help to assess the type of hearing loss and also to compare both ears. Clinically, deafness may be classified as sensorineural and conductive. Deafness caused by impairment of conduction along the neural path is termed sensorineural deafness. Conductive deafness is caused by defective conduction of vibration to the internal ear often by diseases of the middle ear and ossicles. Tuning fork of frequency 512 Hz is preferable since the notes of higher frequency forks tend to decay quickly not



Figs 52.13A and B: Rinne's test (A) Air conduction, (B) Bone conduction

allowing sufficient time for the test to be performed and lower frequency forks tend to enhance perception by the sense of vibration.

Rinne's Test

The tuning fork is held in the right hand by the stem and activated. It is placed over the mastoid process while the patient's head is steadied with the left hand. The patient is asked to indicate when the sound disappears and the fork is immediately held erect and in line with the external auditory meatus about 2 cm away. If the patient still hears the note, the test is over and Rinne is termed positive. If the patient does not hear the note, the test is reversed. The vibrating tuning fork is held 2 cm away from the external auditory canal and till the patient stops hearing (Fig. 52.13A). Then the base of the tuning fork is applied over the mastoid process. (Fig. 52.13B). If the patient starts to hear the note, Rinne is termed negative, i.e. bone conduction is better than air conduction. If the tuning fork test shows that air conduction and bone conduction are equal, then Rinne is termed equal or equivocal.

- *Interpretation* Normal or sensorineural deafness
- Rinne positive
- Rinne negative Conductive deafness
- Rinne equal Very mild conductive deafness of less than 20 dB

False Negative Rinne

In unilateral severe sensorineural deafness while testing with a tuning fork, the patient may indicate that bone conduction is better than air conduction in the diseased side.



Fig. 52.14: Weber's test

This is false negative Rinne. The sound is heard by the opposite normal ear by vibrations passing through the skull to reach it. This can be avoided by masking the normal ear.

Weber's Test

The base of a vibrating tuning fork is placed over the vertex or middle of forehead just above the glabella and the patient is asked to indicate the site at which the note is heard. A normal person hears the note equally on both sides, so that he feels that it is heard in the midpoint of the forehead. This is termed "Weber is central". When the note is heard better in either ear it is termed "Weber is lateralized" to right of left, as the case may be (Fig. 52.14).

Interpretation: *Normal*—A person hears equally on both sides or does not hear bone conduction at all if the room is noisy. In unilateral conductive deafness, the Weber is lateralized to the diseased ear and in bilateral conductive deafness Weber is lateralized to the more affected ear. In unilateral

sensorineural deafness, Weber is lateralized to normal side and in bilateral sensorineural deafness, Weber is lateralized to the less affected side. To distinguish the cause of abnormal Weber's test, Rinne test is also performed simultaneously.

Clinical Example:

Weber's test is lateralized to the right, i.e. heard better in the right ear.

This can be either due to conductive deafness in the right ear or sensorineural deafness in the left. In the former situation, Rinne will be negative on the right side whereas in the latter it will be positive on both sides.

Absolute Bone Conduction Test

The base of the vibrating tuning fork is placed over the mastoid process of the patient and the external canal is occluded by the finger. The patient is instructed to raise his finger when he stops hearing the sound. Then, the examiner places the tuning fork onto his own mastoid process and occludes the external auditory canal. If the examiner still hears the note, the absolute bone conduction of the patient is reduced (provided the examiner's hearing is normal).

Interpretation

Absolute bone conduction (ABC) of the patient is equal to that of the examiner.

Conductive deafness: *ABC* of patient is the same as that of the examiner.

Sensorineural Deafness

ABC of the patient is less than that of the examiner. There are several other tuning fork tests like Bing test, Gelle test, Escat test and Bonnier test, which are not routinely performed.

Psychogenic Deafness

To detect psychogenic deafness various tests like Chimanimoos test, Doorfler Stewart test, Stenger test, Lombard's test, Erhard's test and others can be performed.

EXAMINATION OF NOSE

Inspection

Look for deformities of the nose. The tip of the nose is elevated with the thumb and the vestibule is inspected with the light focussed on to it (Fig. 52.15).



Fig. 52.15: Inspection of nose

Abnormalities in the vestibule of nose and displacement of septum can be made out. Papilloma, cysts, bleeding points in the anterior end of nasal septum and other abnormalities can be made out better by direct examination since these lesions may be obscured by the blades of the nasal speculum on rhinoscopy.

Fracture of nasal bones is detected by palpation of the dorsum of the nose. Lateral movement of the nasal bones brings out crepitus.

Anterior Rhinoscopy

This is done with a nasal speculum. Thudichum's (Fig. 52.16), Duplay's (Fig. 52.17), or St Clair Thomson's nasal speculum can be used. The speculum is introduced into the nostril and the light is directed into the nasal cavity.

The septum, nose, floor of the nose, inferior meatus and turbinate and middle meatus and turbinate are carefully examined. The degree of patency of each side, the color of the mucous membrane, presence of mucus, pus or crusts in the nose, and any other lesion are noted. If any mass is seen in the nose, it is gently palpated with a cotton bud, to know its attachment, consistency, sensitivity to touch and tendency to bleed. In children with history of unilateral foul smelling discharge, foreign body or a rhinolith may be detected. Nasal polyp is seen as a bluish grey, smooth, shining mass which is mobile and insensitive to touch. *Rhinosporidiosis* is seen as reddish irregular mass with white dots over the surface, which are sensitive and bleed on touch. Carcinoma of the nose and paranasal sinuses appear as firm, fleshy masses. Hematoma and abscess present as bilateral fluctuant swellings in the anterior part of the nasal septum.



Fig. 52.16: Anterior rhinoscopy using Thudichum's speculum



Fig. 52.17: Anterior rhinoscopy using Dupley's speculum

Nasal Airway Patency Test

A cotton wool is placed in front of one anterior nares while the other is occluded by pressing over the *ala nasi* with the finger. The movement of cotton wool by the expired air gives an idea of the degree of nasal obstruction. The severity of obstruction on either side can be compared by holding a cold tongue depressor below the nostrils and noting the areas of fogging on the tongue depressor while the patient gently exhales through the nose.

Tests for Smell Sensation

Bottles containing clove oil, peppermint oil and tincture asafoetida are used as test substances.

Any other familiar substance can be used depending on the circumstances. Each nostril is tested separately. One nostril is closed by finger and the bottles are brought to the open nostril one by one and the patient is asked to recognize the smell of each substance separately. After this, the other nostril is tested. It is preferable to instruct the patient to close his eyes, to avoid visual identification. Irritants such as ammonia and substances with strong pungent odor tend to mask the sensation of smell for variable periods. Hence, these have to be avoided.

Rhinomanometry

The study of nasal pressure and flow is called rhinomanometry. Active rhinomanometry is the recording of nasal air flow and pressure with normal breathing. Passive rhinomanometry is generation of nasal air flow and pressure from an external source such as a fan or a pump to drive in air into the nose. Nasal resistance motors are now available and some of the more modem equipments incorprate a micro-computer to process and store the information.

Olfactory Spectrogram

The seven primary odours-camphoraceous, ethereal, floral, musky, minty, pungent and putridare used to test the sense of smell qualitatively and quantitatively. The dissolved substances are placed in bottles and the air above the solution is blown into the nose by a syringe. The volumetric quantity of air required to produce sensation of smell is recorded for each substance.

This test helps to compare one nostril with the other and one patient with another, and also to assess the progress of the disease (Fig. 52.18).

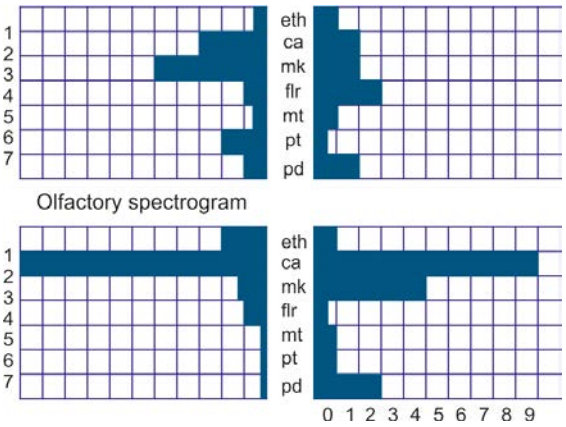


Fig. 52.18: Olfactory spectrogram normal and with anosmic zones:

1. (Eth)-Ethereal
2. (ca)-camphoraceous
3. (mk)-musky
4. (flr)-floral
5. (mt)-minty
6. (pt)-pungent
7. (pd)-putrid

Note: The anosmic zone for the particular smell is represented by the shaded area.

Loss of sense of smell is called anosmia. Any disorder of perception of the sense of smell is called parosmia. It may be a false sense of odors or perception of those which do not exist. Anosmia may be due to local abnormalities in the nose or abnormalities of the neurological mechanism of olfaction (olfactory nerves and its connections). Neurological causes are further, described in Chapter 32. Local conditions include rhinitis, blocking of nose, fracture of base of skull and similar causes. While attributing anosmia to neurological cause, all such local conditions should be ruled out.

Examination of Paranasal Sinuses

Inspection

Empyema, mucocele and tumors of frontal sinus may reveal obvious swelling over the forehead which can be easily made out. Inflammation or tumors of the maxillary sinus may produce swelling of the face lateral to the nose. Swelling medial to the medial canthus of the eye may be caused by pathology of the ethmoid.

Palpation

Inflammation of the paranasal sinuses can be detected by eliciting tenderness on palpation.

Maxillary Sinuses

Tenderness over the maxillary sinuses can be elicited by pressing over the canine fossa on the cheek, with forefinger on one side and the middle finger on the other, and then noting the facial expression of the patient and comparing the pain experienced on either side (Fig. 52.19).

The infraorbital rim can then be palpated for any step deformity (as in fractures) or for blunting as occurs in malignancy of the maxillary sinus. Palpate the anterolateral wall of the maxillary antrum for irregularity or bulge.

Frontal Sinuses

In case of frontal sinusitis, tenderness is elicited by pressing over the floor of the frontal sinus, with forefinger on one side and middle finger on the opposite. Palpation of the supraorbital rim should also be done for any irregularity (Fig. 52.20).

Ethmoid Sinuses

In ethmoid inflammation, tenderness is elicited by pressing on the sides of the nose midway between the inner canthi of the eyes and the nasion.

Transillumination Test

This is performed in a dark room. A lighted bulb is placed in the oral cavity and the patient is asked to close the lips. Normally, an infraorbital crescent appears as a glow below the orbit on either side. In maxillary sinusitis, the sinus becomes opaque and the glow is abolished. For detecting frontal sinusitis, the test is performed by keeping the lighted bulb against the floor of the frontal sinus and noting the glow over the forehead. Both sides are compared.



Fig. 52.19: Eliciting tenderness over the maxillary sinuses



Fig. 52.20: Eliciting tenderness over frontal sinuses

EXAMINATION OF NASOPHARYNX

The procedure is first explained to the patient. A post-nasal mirror is warmed by showing the mirror surface over the flame of a spirit lamp or dipping it in hot water and the metal surface of the mirror is tested against the dorsum of the examiner's hand, to ascertain that it is not too hot. Warming the mirror avoids fogging by moisture in the patient's breath. The patient is asked to breathe quietly through the nose and relax with the mouth kept open. Using a Lack's tongue depressor the anterior 2/3 of the tongue is depressed with the left hand. The light is focussed on the posterior pharyngeal wall just below the uvula. The warmed postnasal mirror is held in the right hand and passed into the oropharynx between the posterior pharyngeal wall and soft palate without touching either (Fig. 52.21).

The posterior end of the septum is seen as a vertical edge. On either side of the posterior end of septum, the choanae are seen. The posterior edges of the inferior and middle turbinates are seen on the lateral side of the nasal cavity. Posterior end of superior turbinate is rather difficult to visualize.

Hypertrophied posterior end of inferior turbinate appears as rounded, mulberry-like swellings on each side in the choanae. Discharge may be seen trickling from the meati over the ends of the turbinates. Abnormalities such as antero-choanal polyp will be seen as a greyish smooth swellings coming out of the choanna into the nasopharynx. A lateral tilt of the mirror brings the lateral wall of the nasopharynx into view. The eustachian tube opening and tubal elevation can be visualized. Above and behind the tubal elevation

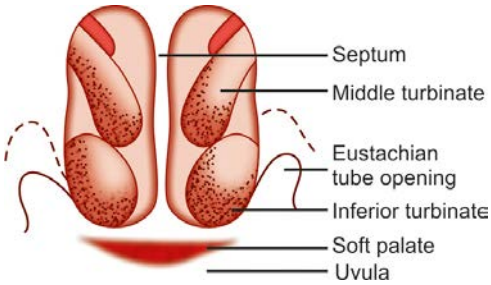


Fig. 52.22: Diagram of structures seen in posterior rhinoscopy

is the fossa of Rossenmuller which is a frequent site of malignancy (Fig. 52.22).

The roof and posterior wall of nasopharynx are visualized next. Adenoid tissue is seen as a pinkish mass with vertical grooves over the surface at the junction of the roof and posterior wall of nasopharynx. Nasopharyngeal fibroma appears as a red, lobulated mass with prominent vessels. Nasopharyngeal cancer appears as a proliferative or ulcerative lesion. In some hypersensitive patients, pharynx may have to be anesthetised by spraying or painting 4% xylocaine, to avoid retching.

Further examination of nasopharynx is done by fiber optic nasopharyngoscopy or by Yanker's nasopharyngeal speculum.

EXAMINATION OF ORAL CAVITY AND OROPHARYNX

The patient is asked to open the mouth and the light is reflected into the oral cavity (Fig. 52.23)

Lips, cheek, teeth, gums, tongue, floor of mouth and palate are carefully examined for any lesions. Pigmentation of the mucosa, ulcers or growths are all looked for. Patient is asked to put out the tongue



Fig. 52.21: Posterior rhinoscopy



Fig. 52.23: Examination of oral cavity

as far as possible. Note, if there is any restriction of movement and whether the tongue is deviated to any side. The dorsum and the lateral borders of the tongue are inspected. The patient is asked to rotate the tongue up towards the roof of the mouth. This facilitates the examination of its undersurface and the floor of mouth.

Method of Examination of the Oropharynx

The tongue is depressed with a Lack's tongue depressor to bring into view the oropharynx. The tongue depressor should not go beyond the anterior 2/3 of tongue since it will cause the gag reflex. The palatoglossal and palatopharyngeal folds, the tonsils, the tonsillolingual sulcus, posterior pharyngeal wall and palate should be carefully inspected for any lesion. The patient is asked to say" Ah" and the movement of soft palate is noted (Fig. 52.24).

Acute tonsillitis is characterized by congestion of tonsils with white spots over the crypts. Membrane formation over the tonsil may be noticed in diphtheria, streptococcal tonsillitis, and moniliasis. In diphtheria, the membrane is greyish white and firmly adherent to the surface. In streptococcal tonsillitis, the membrane is whitish and can be removed easily. In Vincent's angina, the tonsil suffers much destruction and the membrane extends deeply. A milky white, curd like patch which is easily removable is seen in monilial infection.

Unilateral enlargement of tonsil may suggest tonsillar abscess, tonsillolith or tumor. Tonsil may be pushed medially by parapharyngeal abscess or tumors. A bulge of the posterior pharyngeal wall on one side of the midline in a child with dysphagia and dyspnea is characteristic of an acute retropharyngeal abscess. Cold abscess arising from tuberculosis of cervical vertebrae may be seen as a chronic retropharyngeal abscess in adults.

White horny outgrowths arising from the mucosa of the tonsils and pharynx without any evidence of inflammation are characteristic of keratosis pharyngis.

Carcinoma of the tonsil presents as an ulcer which hard, everted edges, whereas a gumma manifests in the form of a punched out ulcer.



Fig. 52.24: Examination of oropharynx

EXAMINATION OF LARYNX AND LARYNGOPHARYNX

The examination of larynx using a laryngeal mirror is called indirect laryngoscopy. The procedure is explained to the patient who is seated directly facing the examiner.

The patient protrudes the tongue as far as possible after removing dentures if any. The light is focused into the patient's mouth. The examiner holds the protruded tongue firmly with a gauze strip between the thumb and middle finger of the left hand, while the index finger of the same hand is kept resting against the upper teeth for steadying the face and for retracting the upper lip. The patient is asked to breathe gently and a warmed laryngeal mirror of appropriate size, held in the right hand like a pen with the mirror facing downwards, is introduced into the oral cavity. The mirror is rested against the soft palate without touching the posterior pharyngeal wall.

Posterior part of tongue, vallecula, lingual aspect of epiglottis and its margins are the structures seen first (Fig. 52.25).

By tilting the mirror, the laryngeal aspect of epiglottis, arytenoids, ary-epiglottic folds, the vestibule of larynx, vestibular folds and vocal cords come into view. The vestibular folds appear as dull red bands above the vocal cords. Vocal cords appear as whitish, flat, ribbon-like bands below the vestibular folds. The patient is asked to say "ee" or "eh" when the movement of vocal cords can be seen. Below the vocal cords, the walls of subglottis are hidden from view but a few rings of trachea may be

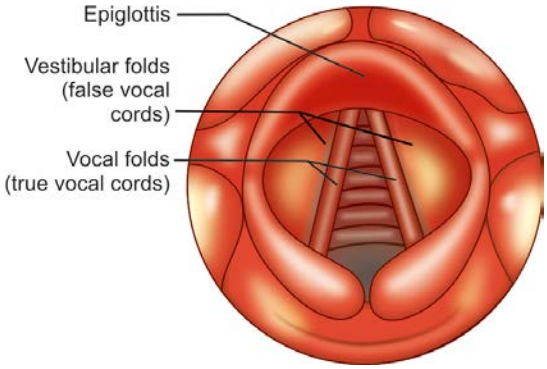


Fig. 52.25: Indirect laringoscopy—structure seen in indirect laryngoscopy: epiglottis, vocal cords, rima glottidis, and pyriform fossa

seen anteriorly. By tilting the mirror suitably the adjacent pharyngeal walls can be inspected. If the patient gags or retches, the posterior pharyngeal wall is anesthetized by spraying 4% xylocaine. In obese patients with short neck indirect laryngoscopy is difficult to perform.

In unilateral recurrent laryngeal nerve paralysis the ipsilateral vocal cord assumes a median or paramedian position and does not move laterally on deep inspiration. Some of these patients may be asymptomatic whereas others may have dysphonia. In many cases, the voice usually improves due to compensation by the healthy cord which crosses the midline to restore the rima glottidis.

In bilateral abductor paralysis, the vocal cords lie in median or paramedian position and the air way is inadequate leading to dyspnea and stridor on exertion; but the voice will be good. These patients will require permanent tracheostomy with speaking valve or surgical procedure to lateralize the cords. In idiopathic bilateral abductor paralysis, since the voice is good the condition may remain undiagnosed for long, being treated as cases of bronchial asthma on account of the dyspnea and noisy breathing especially during sleep. The diagnosis is made only when examination of larynx is undertaken.

Palpation of the Larynx

The larynx should be palpated to detect widening of the thyroid cartilage. Growths in pyriform fossa or laryngeal growths extending beyond the larynx lead to widening. Mobility of the larynx over prevertebral fasica is detected by grasping the thyroid cartilage between thumb and index finger and moving it from side to side. The gritty sensation created by this maneuver (crepitus) is abolished in lesions which push the larynx forwards away from the prevertebral fascia, e.g. retropharyngeal abscess and postcricoid malignancy.

CHAPTER

53 Special Investigations in ENT Diseases

OS Radhakrishna Pillai

Assessment of auditory function, Subjective audiometry, Impedance audiometry, Evoked responses in audiometry, Assessment of vestibular functions, Bacteriological examination, Radiology, Magnetic resonance imaging, Biopsy, Stroboscopy and cinephotography, endoscopy, Polysomnography

Aim of investigations is to confirm the diagnosis, quantitate the loss of function, establish the etiology of the diseases and plan the treatment modalities.

ASSESSMENT OF AUDITORY FUNCTION

Audiometry

Audiometer is an electrical instrument used to measure hearing threshold at various frequencies. Subjective and objective audiometry help to diagnose the type and degree of deafness and locate the site of lesion.

Subjective Audiometry

Pure Tone Audiometry

The threshold of hearing by air conduction and bone conduction for frequencies—125, 250, 500, 1000, 2000, 3000, 4000, 6000, and 8000 Hz is determined. The examiner applies a sound stimulus and gradually increases its intensity till it is heard by the subject. An alternative method is to apply to the ear a sound that is readily heard and gradually decreasing it till it disappears. The test is performed with sounds of different frequencies. The lowest intensity at which the subject hears the sound is marked as the threshold at that frequency. Both air conduction and bone conduction are studied. The audiogram is a graphic record of the hearing threshold at different frequencies (Figs 53.1 to 53.3).

Symbols used in audiogram are given in Table 53.1

Table 53.1: Symbols used in audiograms

Modality	*Ear*	
	Right	Left
Air conduction unmasked	O	X
Air conduction masked	Δ	□
Bone conduction unmasked	<	>
Bone conduction masked	[	]
No response		

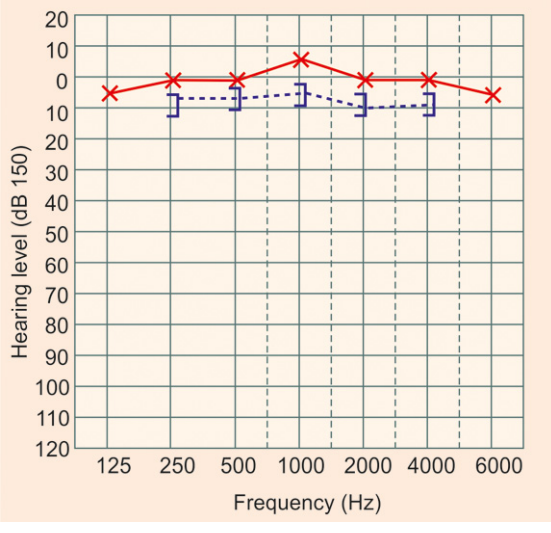


Fig. 53.1: Pure tone audiogram—normal X-air conduction, (]-bone conduction)

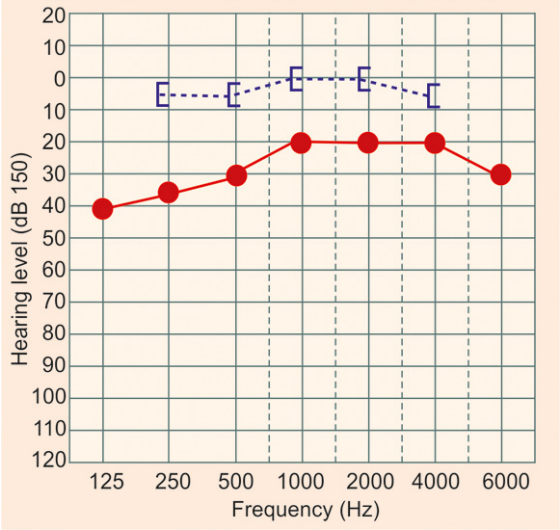


Fig. 53.2: Conductive deafness right ear

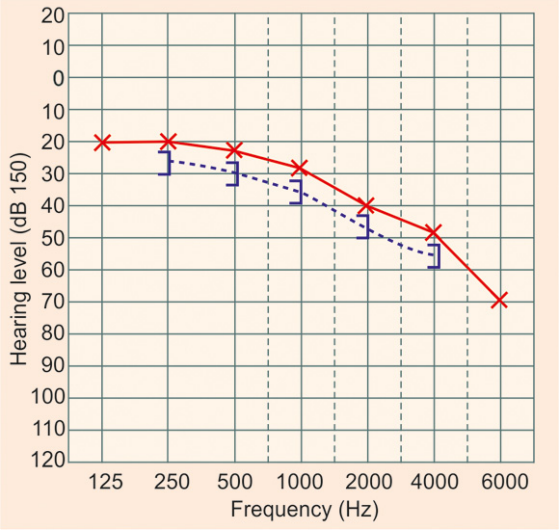


Fig. 53.3: Sensorineural deafness of left ear

Observation

Normally both air and bone conduction curves superimpose on the graph. The range of 0–20 dB is considered as normal threshold for hearing.

In conductive deafness, the audiogram will show impairment of air conduction while bone conduction will be normal. In sensorineural type of deafness both air and bone conduction curves show equal loss of hearing.

Speech Audiometry

Clinical speech audiometry records word-identification scores for a set of prerecorded words, given at different intensity levels. Reception threshold and discrimination of speech are measured.

Speech Reception Threshold

Spondee words which are words with two syllables, both pronounced with equal stress are used, e.g. sunset, seashore, horse-shoe, tooth brush, farewell, etc. The intensity at which the patient identifies and correctly repeats 50% of the words, is called speech reception threshold.

Speech Discrimination

This is tested by using phonetically balanced words which are mono syllables, e.g. cat and bat, sit and hit. These words are presented at an intensity about 25 dB greater than the individual's speech reception threshold. The percentage of words that the patient can repeat correctly is his discrimination score or phonetically balanced score.

Information Gained by Speech Audiometry

This test helps to localize the lesion in the auditory pathway. Speech discrimination is good in conductive deafness. It is poor in retrocochlear lesions but better in cochlear lesions.

In addition, the response to hearing aids can be predicted and the improvement with auditory training can be assessed.

Alternate Binaural Loudness Balance Test

This test is used to detect recruitment in unilateral deafness. Recruitment is a phenomenon in which the ear which does not hear low intensity sounds, will hear higher intensity sounds as loud or even louder than the normally hearing ear. A tone is presented alternately to the normal and affected ear and the intensity in the affected ear is adjusted to match the loudness in the normal ear. In conductive deafness and retrocochlear deafness the initial difference is maintained throughout while in cochlear deafness recruitment is seen.

Patients with cochlear deafness distinguish smaller changes in intensity of pure tones better than those with conductive or retrocochlear deafness.

Speech Audiometry—Alternate Method

Here the percentage of phonetically balanced words correctly heard by the patient at different intensity levels are charted on a graph and two parameters are assessed.

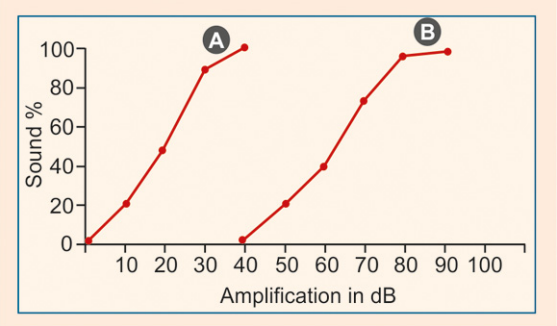


Fig. 53.4A: Calculation of half peak level. A–normal, B–conductive hearing loss

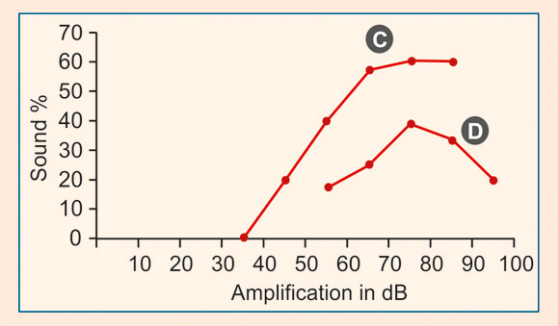


Fig. 53.4B: C-sensorineural hearing loss D-retrocochlear lesion

1. Optimum discrimination score (ODS): This is the highest score irrespective of the intensity level.
2. Half peak level (HPL): This represents the intensity level where 50% of the words are expected to be heard. This is derived from the graph (Figs 53.4A and B).

A. Normal curve ODS is 100% and HPL is 15 dB.
B. Conductive hearing loss of 40 dB. ODS is 100%. While HPL is 55 DB shape of curve is normal. HPL is 40 dB above normal.
C. S N Loss of 40 dB. ODS is 60% and HDL is 55 dB. There is no increase in score beyond 70 dB.
D. This is a roll over curve seen in retrocochlear lesions. ODS is 40% at 80 dB and further increase in intensity causes a drop in the score.

SISI score: Tone is presented 20 dB above the threshold and sustained for about 2 minutes. Every 5 seconds, the tone is increased by one dB and 20 such blips are presented. Patient indicates the blips heard and the percent of blips heard is calculated. This is termed the short increment sensitivity index score (SISI score). In conductive deafness the SISI score is seldom more than 15%. In retrocochlear lesions it is 0 to 15% and in cochlear lesions it is 75 to 100%.

Tone Decay Test

It is a measure of nerve fatigue. It is used to detect retrocochlear lesions. A continuous tone is presented at threshold level for 1 minute. If the patient stops hearing within 60 seconds, increase the intensity by 5 dB till the tone is heard for 60 seconds fully. The number of dB by which the tone has to be raised is noted. In normal and conductive deafness tone decay is 0 to 15 dB while in cochlear lesions it is 20 to 25 dB and in retrocochlear lesions it is above 25 dB.

Bekesy Audiometry

This is done by an automatic audiometer, which scans the patient's threshold to both continuous and interrupted sound stimulus. The record may show one of five patterns.

Type I Thresholds for the continuous and interrupted sound stimuli overlap. This is normal or may also be seen in conductive hearing loss.

Type II The continuous and interrupted tracings overlap at lower frequencies, but at around 1000 Hz, the continuous tracing runs below the interrupted tracing, and then runs parallel to it. Such a curve is seen in some cases of sensorineural deafness.

Type III The continuous graph dips abruptly from the interrupted tracing before 500 Hz. This signifies retrocochlear lesions.

Type IV The continuous graph remains below the interrupted tracing from the start. This is seen in some types of retrocochlear lesions.

Type V Here the continuous tracing runs above the interrupted tracing. This is suggestive of hysterical deafness (Figs 53.5 to 53.9).

Impedance Audiometry

In this form of audiometry, the impedance or resistance offered to sound by the middle ear conducting mechanism is assessed. The sounds

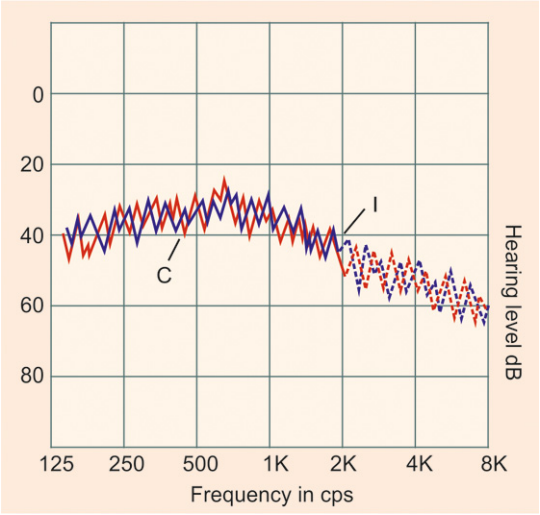


Fig. 53.5: Bekesy audiogram–Type I (I–intermittent, C–continuous)

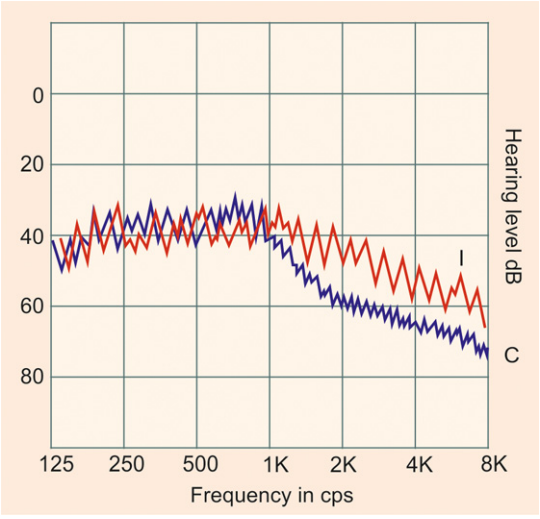


Fig. 53.6: Bekesy audiogram–Type 2

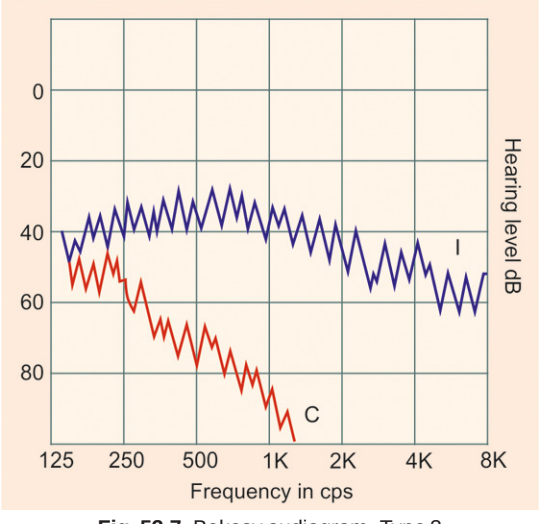


Fig. 53.7: Bekesy audiogram–Type 3

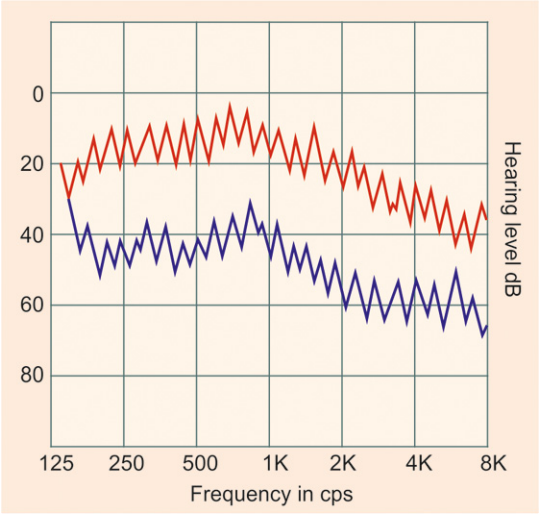


Fig. 53.8: Bekesy audiogram–Type 4

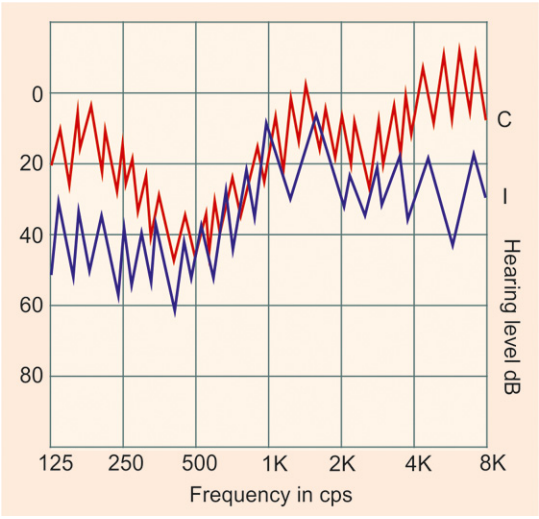


Fig. 53.9: Bekesy audiogram–Type 5

reflected from the tympanic membrane are measured. The changes in impedance of the middle ear are determined for varying pressures in the external auditory canal. The resultant graph is called a tympanogram. This type of audiometry helps to diagnose various middle ear diseases like secretory otitis media, adhesive otitis media, ossicular chain disruption and otosclerosis. Automatic impedance audiometers are available at present which scan middle ear compliance.

The tests performed by this method are:

1. Tympanometry
2. Measurement of acoustic impedance, and
3. Estimation of acoustic reflex threshold. Impedance audiometry helps to identify the various causes of conductive deafness (Figs 53.10 to 53.14).

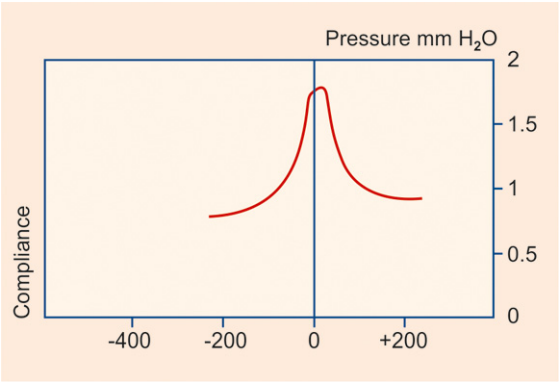


Fig. 53.10: Tympanogram normal–Type A

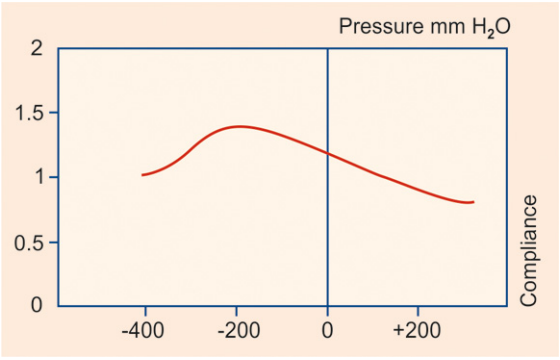


Fig. 53.11: Tympanogram reduced middle ear pressure–Type C

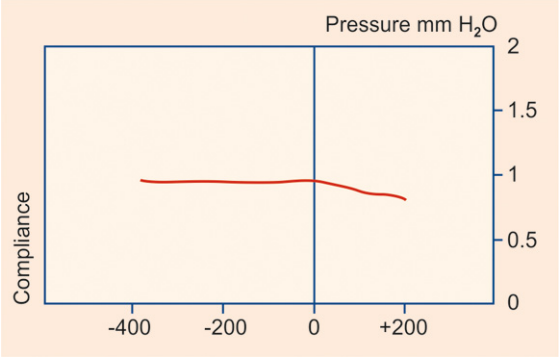


Fig. 53.12: Tympanogram fluid in the middle ear

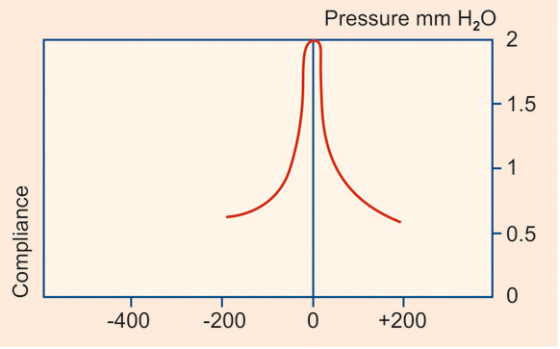


Fig. 53.13: Tympanogram ossicular disruption–Type Ad

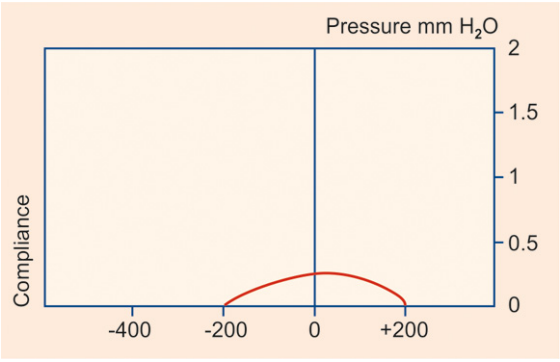


Fig. 53.14: Tympanogram otosclerosis–Type As

Psychogalvanic Skin Resistance Audiometry

This test is performed to assess the responses to acoustic stimulus. This is based on a conditioned reflex. By applying a pure tone stimulus followed by a painful stimulus repeatedly, the patient is conditioned in such a way that the pure tone stimulus alone will produce the same kind of galvanic response that is produced by the painful stimulus. Anticipation of a painful stimulus after each pure tone stimulus causes slight sweating and this increases the flow of current between two electrodes placed suitably.

Auditory signal is presented to one ear usually through an ear phone. Two shock electrodes are placed on the calf of one leg approximately 2.5 cm apart. The pick up electrodes are placed on the soles of the feet or on both surfaces of the same foot. The response is registered on a voltmeter in a wave form. This test can be performed even in infants and young children. Infants in arms are tested with the mother holding the baby.

Evoked Responses Audiometry

Electrocochleography

It is a measurement of potentials arising within the cochlea and auditory nerve, i.e. the cochlear microphonics, the summating potential, and action potentials of the eighth cranial nerve. In most cases, one electrode has to be placed through the tympanic membrane onto the bone of the promontory to make these recordings, although ear canal recording is possible in many cases.

Brainstem evoked response audiometry (BERA): This test measures the electrical activity in the auditory pathways and is a completely objective test.

Electrodes attached to the forehead and mastoid process record the electrical responses evoked by sound stimuli. A series of rapid sounds (about 25 per second) provide the stimulus. Events are recorded during the first 10 milliseconds following the auditory stimulus. In a normal person, seven waves are produced in the first 10 milliseconds. The first, third and fifth waves are most stable. The absolute peak latency for waves, I, II, III, IV, and V, interpeak latency of I-III, III-V and I-V are used for clinical interpretation. The exact anatomic site of origin of waves is still disputed, but they are thought to arise from the following parts:

- Wave I - VIII nerve
- Wave II - Cochlear nuclei
- Wave III - Superior olivary complex
- Wave IV - Lateral lemniscus
- Wave V - Inferior colliculus
- Wave VI - Medial geniculate body
- Wave VII - Auditory radiations

Measurement of latency from the stimulus to the appearance of waveforms and the characteristic wave-form patterns are compared with normal patterns. Variations in the patterns help to identify and localize the lesions. Brainstem evoked audiometry has its greatest use in the diagnosis of retrocochlear lesions and nonorganic hearing loss. This test can be done on infants and this is a great advantage. BERA is now an established method of hearing assessment in neonates and infants.

Cortical Evoked Response Audiometry

This records the electrical activity occurring in the cortex caused by sound stimuli. The active electrode is placed on the vertex of the head and reference electrode on the mastoid process. This test can be performed only in adults and older children.

Evoked Otoacoustic Emission Test

This is a test intended to detect hearing loss even in neonates and infants. Otoacoustic emissions are low level sounds produced by the internal ear even if it is not stimulated. When the ear is stimulated by external sound stimuli these otoacoustic emissions become more apparent. These are called transient evoked otoacoustic emissions. Recording of these echo sounds and their interpretation enable the detection of cochlear lesions even in neonates.

ASSESSMENT OF VESTIBULAR FUNCTIONS

Fistula Test

Normally the middle ear and inner ear do not communicate directly. In some disease states fistulous communication may develop between them. Presence of such as fistulous communication is detected by the fistula test.

The air in the external auditory canal is compressed by pushing the tragus with a finger or by compressing the bulb of a Siegle's speculum. If the test is positive, the patient experiences vertigo. Nystagmus may occur if the labyrinth is functioning normally. If the labyrinth is damaged, the test will be negative even in the presence of a fistula and this is a "false negative" test. False positive results occur even in the absence of a fistula, if the foot plate of the stapes is abnormally mobile or if there is endolymphatic hydrops. When there is a positive fistula test with an intact tympanic membrane and no evidence of middle ear disease, it is named *Hennobert's sign.* It is seen most commonly in congenital or late tertiary syphilis, rarely it may occur in Meniere's disease also.

Spontaneous Nystagmus

Nystagmus is involuntary rhythmic eye movements. Spontaneous nystagmus is seen in vestibular lesions. It is fine and rotatory with two components—a slow component of vestibular origin and a fast component due to central correcting mechanism. The direction of fast component is taken for assigning the direction of nystagmus. Nystagmus can be graded as follows:

First Degree

Nystagmus is present only when the patient looks towards the side of fast component.

Second Degree

Nystagmus is present when the patient looks straight and towards the direction of fast component as well. Generally vestibular nystagmus does not last for more than 6 weeks.

How to Look for Nystagmus?

Always look for nystagmus under good illumination. First observe the eyes in their primary position. In this position, congenital pendular nystagmus and second degree jerk nystagmus can be detected. The

patient is seated in good light and asked to look straight on to the examiner's finger which is held at least 45 cm away from the nose. The presence of nystagmus is noted viewing from one side. The finger is moved laterally in the same horizontal plane, 30° on either side asking the patient to follow the finger and noting for nystagmus. Spectacles can be worn if the patient regularly uses them. The next step is to abolish visual fixation by using *Frenzle's glasses*. It is also possible to abolish fixation by performing the test in a dark room, where eye movements can be observed with an infrared viewer. Horizontal nystagmus is detected in these two positions. Vertical nystagmus can be detected by asking the patient to look at your finger held at a level just above or below the level of the primary position of the eyes. A special type of vertical nystagmus called down-beat nystagmus (see below) is brought out prominently in the lateral gaze position of the eyes.

Note: While testing for nystagmus, the finger should not be held too close to the patient's eyes so as to avoid the accommodation reflex. Similarly, extremes of gaze should be avoided because even normal individuals may show nystagmus in these positions due to muscle fatigue, especially if the gaze is maintained for more than 30 seconds. Anxious individuals may show nystagmus within 1 to 2 mm of extreme abduction and adduction of the eyes. In both these situations, the oscillatory movements of the eyes will be irregular and ill sustained and they are not pathological, they are more correctly termed as 'nystagmoid' movements.

Generally nystagmus due to peripheral lesions enhances when visual fixation is abolished, and nystagmus due to central lesions reduces. If the labyrinth is irritable or hyperfunctioning on one side, direction of nystagmus is towards the same side. When the labyrinth is hypo-or nonfunctioning the direction of nystagmus is to the opposite side.
(Also refer to chapter 32 Neurology)

Induced Nystagmus

The function of vestibular system may be evaluated by stimulating the labyrinth and noting the responses.

Videonystagmography also known as video–oculography has recently become the preferred method for recording eye movements during vestibular testing.

Caloric Test

In this test the labyrinth is stimulated by changes in temperature (Fig. 53.15).

Fitzgerald-hallpike Bithermal Caloric Test

Both ears are checked for wax and for the presence of perforation. The patient lies supine on a couch with the head elevated to 30° from the horizontal so that the lateral semicircular canal is brought to the vertical plane. Each ear is irrigated by sterile water at 44°C and 30°C with the reservoir kept 60 cm above the patient's ear. About 300 mL of water is used for each irrigation. The nozzle is directed towards tympanic membrane and water is allowed to flow for 40 seconds. Nystagmus is observed with the patient focusing his eyes on a near object. The duration of nystagmus is noted. Then Frenzle's glasses are used to abolish visual fixation. If the nystagmus reappears, the new end point is also noted. The affected ear is stimulated with warm water first. Then the contralateral ear is tested first with warm water and later with cold water. The test is concluded by cold water stimulation of the affected ear. Between each irrigation, rest periods of 7 minutes are allowed. Normally nystagmus occurs for 90 to 140 seconds after the onset of irrigation and it is prolonged by further 40 seconds when visual fixation is abolished.

Interpretation

a. *Normal response:* Equal response in both ears to all four tests.
b. *Canal paresis:* Duration of nystagmus for hot and cold is reduced.



Fig. 53.15: Caloric test-procedure

c. *Canal palsy:* No response to stimulation.
d. *Directional preponderance:* Response is enhanced in a particular direction.

Canal paresis and directional preponderance may occur either singly or in combination. In lesions of posterior part of temporal lobe, directional preponderance will be demonstrated towards the side of lesion (Figs 53.16 to 53.18).

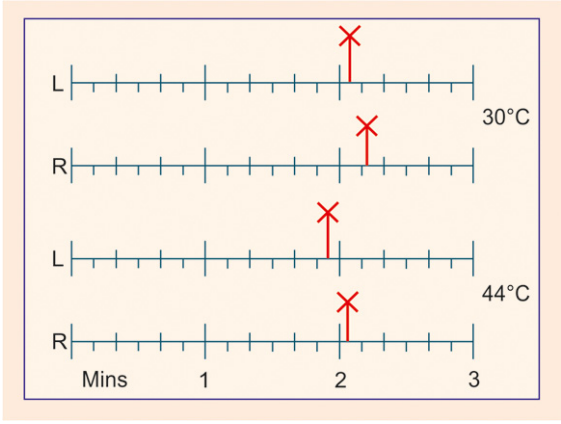


Fig. 53.16: Calorigram—normal caloric response

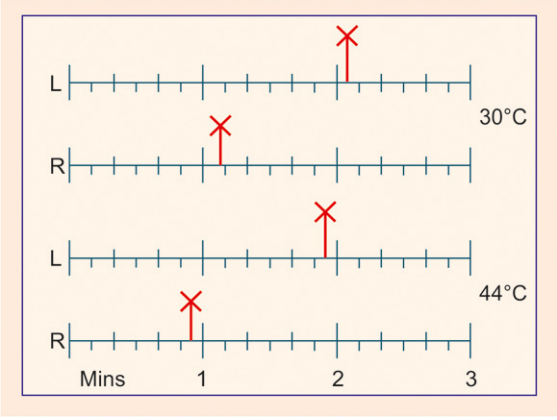


Fig. 53.17: Calorigram—right canal paresis

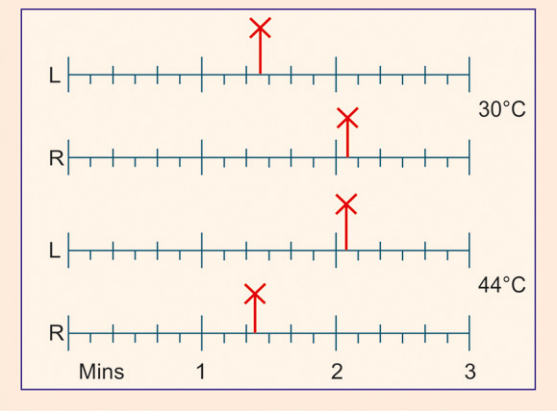


Fig. 53.18: Calorigram—directional preponderance to left

Cold Caloric Test

This test is also done with patient lying on a couch in supine position with the head tilted at 30° to the horizontal. Alternatively patient may be seated in a chair and head tilted backward to 60° from the horizontal plane. Five mL of ice-cold water is introduced into the external auditory canal through a rubber tubing connected to a 10 mL hypodermic syringe and nystagmus is looked for. Normal response is the development of nystagmus which persists for 2 minutes when 5 mL of ice-cold water is syringed into the canal. If nystagmus does not develop with 5 mL, the test is repeated with 10 mL, 20 mL and finally with 40 mL of ice-cold water. Absence of responses to 5 mL, but occurrence of nystagmus with larger quantities of ice-cold water suggest hypoactivity of the labyrinth. Absence of nystagmus even with 40 mL of ice-cold water denotes complete absence of vestibular responses.

Dundas-Grant Test

If the patient has perforation of the tympanic membrane, cold air or oxygen is used instead of ice-cold water to stimulate the labyrinth.

Hypoactive vestibular response occurs in toxicity due to streptomycin, serous labyrinthitis, Meniere's disease, labyrinthine concussion, acoustic neuroma and sometimes after mumps.

Positional Test

Positional nystagmus can be induced by placing the patient's head in different positions. Patient is seated on a couch in such a way that when he lies supine his head will extend beyond its edge. The procedure is explained to the patient. His head is turned 90° to the right or left, and he is asked to lie down quickly, the examiner holds his head turned to right or left, 30° below the horizontal. This position is maintained for 30 seconds. If nystagmus occurs, its latency, direction, duration and fatigability are all noted. Then the patient is asked to sit up quickly while the examiner who holds the head brings it straight so that the patient can look straight. Again nystagmus is looked for. Fine, horizontal, fatigable nystagmus occurs in vestibular lesions and benign positional vertigo. Rotatory or horizonto-rotatory nystagmus is seen in central lesions (Figs 53.19A and B).

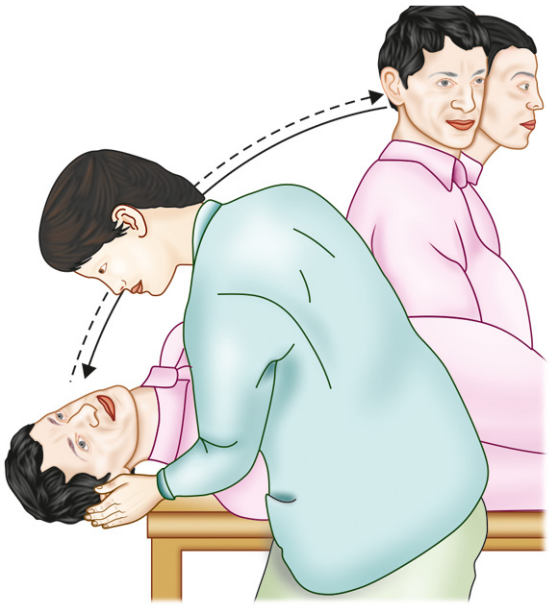


Fig. 53.19A: Cawthorn's maneuver—subject's head turned to right



Fig. 53.19B: Cawthorn's maneuver—subject's head turned to left

Rotation Test

The patient is seated in a barany's chair with head tilted 30° forward so that the lateral semicircular canals are horizontal, and eyes closed, and the chair is rotated ten complete circles in 20 seconds and suddenly stopped and the post-rotation nystagmus is noted. Nystagmus develops in a direction opposite to the direction of rotation, i.e. when rotation is clockwise, nystagmus is to the left. The duration of post-rotation nystagmus is noted. Normally nystagmus persists for 15 to 30 seconds. The disadvantage of the rotational test is that both the labyrinths are simultaneously stimulated.

Optokinetic Nystagmus

The patient is seated on a chair looking at a white drum with black vertical lines kept 90 cm in front. It is rotated in one direction and stopped suddenly and nystagmus is looked for. The test is repeated with the drum rotating in opposite direction. When the drum is rotated clockwise nystagmus is to the right and vice versa. In central vestibular lesions the nystagmus to one side is suppressed.

Cupulometry

This is a type of rotation test performed in the dark, in which nystagmus resulting from rotation is recorded electrically and the subjective sensation of vertigo is also noted.

Electronystagmography

This is electrical recording of nystagmus based on the changes in the corneo-retinal potentials.

Electronystagmogram

An electrode is placed lateral to each eye with a ground electrode placed on the forehead. Because of voltage differences between the cornea and the retina, eye movements can be recorded on a strip chart recorder.

Electronystagmogram (ENG) permits monitoring of nystagmus with eyes closed when suppression is less likely. Characteristic patterns are seen in peripheral and central vestibular disorders, congenital nystagmus and cerebellar lesions. ENG provides a permanent record of nystagmus for medicolegal purposes, for accurate objective calculation of test results, and for the monitoring of treatment. It also helps to differentiate between the normal and abnormal vestibular responses of each side separately (Figs 53.20 and 53.21).

Assessment of Utricular Function

The current technique for assessing function of each utricle is the unilateral centrifugation test. In this

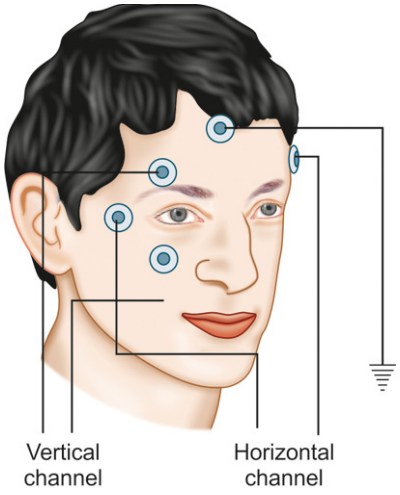


Fig. 53.20: Lead positions for ENG

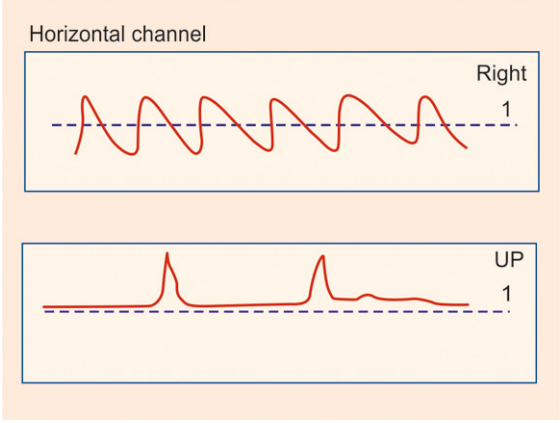


Fig. 53.21: Normal electronystagmogram (ENG)

test the subject is rotated about an "earth vertical axis" at a velocity of 300° to 400°/sec. During the ongoing rotation the subject is gradually translated (shifted) 3.5 to 4 cm first to the right and then to the left along an interaural axis, to a position at which one utricle becomes aligned with the axis of rotation and at this point it is subjected only to gravitational forces. This stimulus induces ocular counter-rolling which reflects the otolithocular reflex. The ocular counter-rolling is measured using videooculography. Signs of dominance of one or the other utricle can be detected from high speed rotation.

Assessment of the Saccule—Vestibular Evoked Myogenic Potentials

The myogenic potentials from the tonically contracted sternocleidomastoid muscle in response to loud sound delivered to the ear are measured. The Vestibular Evoked Myogenic Potentials (VEMP) wave form is biphasic containing positive and negative peaks, occurring after a latency of approximately 13 and 23 msec respectively. These are generated by activation of afferents from the saccules. The instruments required include calibrated sound generators, averaging equipments and surface recording electrodes.

Galvanic Stimulation

Galvanic stimulation delivered by electrodes placed on the mastoids modulates the spontaneous discharge rate of the vestibular afferents of all the vestibular end organs. This produces various behavioral responses such as postural changes, eye movements and perception of movement. It enables identification of vestibular asymmetry.

BACTERIOLOGICAL EXAMINATION

Swabs collected from the ear, nose, throat can be subjected to microbiological tests to identify the infecting agent and determine the sensitivity to antimicrobial drugs.

RADIOLOGY

Ear Diseases

Plain radiographs of the temporal bone reveal the extent of mastoid disease, the condition of the ossicles and extent of pneumatization. Several special views are available to demonstrate different portions of the temporal bone and middle ear. Towne's view and transorbital view of the petrous temporal bone are commonly taken in suspected cases of acoustic neuroma to demonstrate enlargement of the internal auditory meatus (Fig. 53.22).

Nose and Paranasal Sinuses

For the nasal bones a lateral view is taken by placing a dental film in direct contact with the side of the nose and centering the incident beam horizontally through the nose. This can be supplemented by a craniocaudal projection obtained by inserting an occlusal film between the teeth.

For paranasal sinuses occipitomental view (Water's view) is usually preferred. Occipito-frontal, submentovertical, lateral and oblique views may be taken if needed, depending on the site of pathology. Sinusitis gives rise to haziness of the

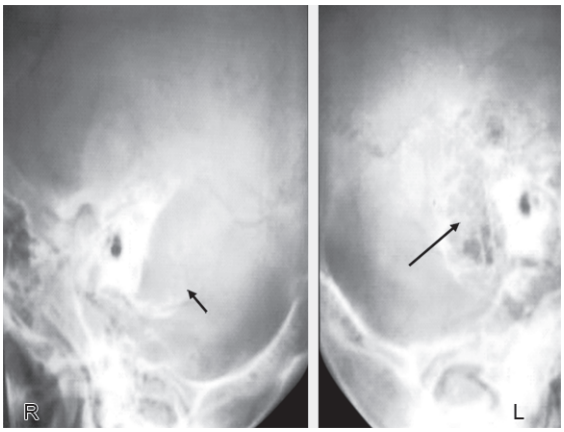


Fig. 53.22: X-rays lateral view of skull for normal mastoid air-cells—arrow points to normal on the left L. X-rays lateral view of skull mastoiditis—arrow point to sclerosed mastoid air cells

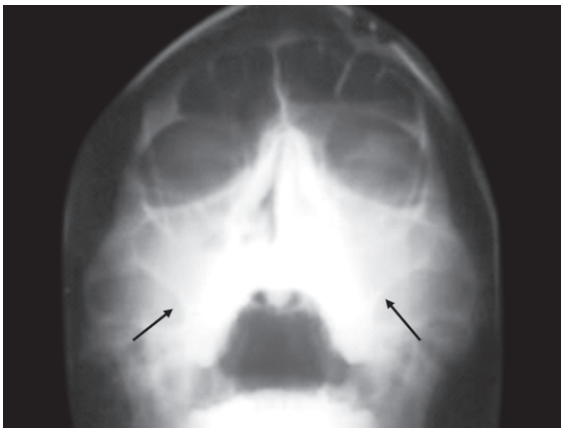


Fig. 53.24: X-ray Bilateral maxillary sinusitis. *Note:* Bilateral opacity of the sinuses (arrows)

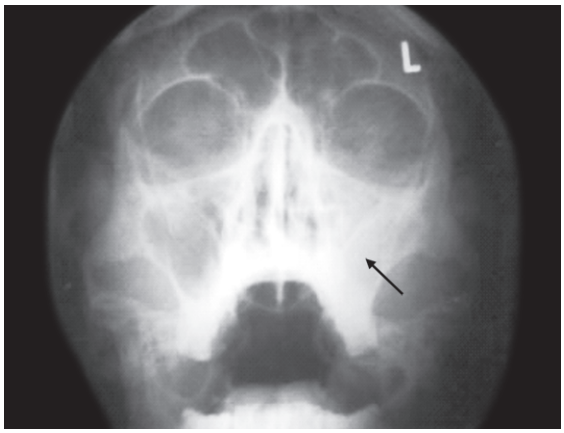


Fig. 53.23: X-ray maxillary sinusitis left *Note:* Opacity caused by exudate filled maxillary sinus (arrow). Right side is normal

sinus without bone erosion. Frontal mucocele reveals loss of scalloping of frontal sinus. Malignancy of sinuses is associated with bone erosion (Figs 53.23 and 53.24).

Nasopharyngeal lesions show up as soft tissue masses obstructing the airway or eroding the base of skull, in the submentovertical views of the skull.

Pharynx and Larynx

Plain radiograph of the lateral view of the neck brings out the cervical spine as well as the pharynx. Caries spine and other lesions of cervical vertebrae can be easily detected. Retropharyngeal abscess is usually seen as widening of the prevertebral space, with air fluid level at times and with straightening of the anterior border of the vertebral column. For demonstration of elongated styloid process an anterioposterior film may be taken with the mouth open.

Foreign bodies in larynx or trachea and tumors occluding the airway can be made out easily.

In laryngeal lesions, skiagram of the chest should be taken to exclude pulmonary tuberculosis, bronchogenic carcinoma, mediastinal tumors, foreign bodies in tracheobronchial tree, and cardiomegaly.

Tomogram

Conventional tomography can demonstrate lesions in the paranasal sinuses, vocal cords, vestibular bands and laryngeal masses. Conventional tomography has been replaced by computed tomography at present.

Laryngogram

After anaesthetizing the larynx, 10 cc of an oil based iodine contrast medium is dropped slowly over the tongue into the larynx and frontal and lateral view skiagrams of larynx are taken during phonation, inspiration and valsalva's maneuver. Laryngogram will give information as to the site, size and extent of laryngeal pathology.

Computed Tomography

CT Scan

Computed tomography helps to pinpoint ear lesions such as tumors and abscesses and also to note intracranial complications.

This is of immense value in diagnosis of lesions of the paranasal sinuses, by demonstrating clearly the osteomeatal complex, thereby aiding functional endoscopic surgery. The bony walls of the sinuses, soft tissue masses and the extension of diseases beyond the bony boundaries are demonstrated clearly. In cases of lesions of nasopharynx CT helps to demonstrate the masses as well as erosion of the base of the skull. CT scan is helpful to give accurate assessment of laryngeal anatomy, to note the extent of tumors of larynx, fractures of hyoid bone or laryngeal cartilages and displacement of arytenoids. CT scan with contrast enhancement is particularly useful in the diagnosis of nasopharyngeal angiofibroma and glomus jugulare tumors.

MAGNETIC RESONANCE IMAGING

It is superior to CT scan in some ways. Fractures are better visualized, and tumors and lymph nodes are differentiated better from muscles and blood vessels. Arteries and veins can also be differentiated.

Magnetic resonance imaging (MRI) can differentiate tumor tissue from retained fluid within the sinus. The extension of sinus neoplasia into cranial cavity is clearly brought out. Nasopharyngeal lesions can also be delineated clearly.

MRI of the larynx can give correct information regarding extent of tumor spread.

Angiography

It is a useful procedure in nasopharyngeal angio fibroma and glomus jugulare tumors. It also facilitates preoperative embolization of the feeding vessel.

BIOPSY

This will be required when patient presents with granulomas, polyps or growth in the ear, nose or throat.

STROBOSCOPY AND CINEPHOTOGRAPHY

The vibration of vocal cords can be visualized and analyzed by means of a stroboscope which provides an interrupted source of light and adjusts the frequency of light interruption to the note produced by the larynx. Cinephotography has also been used for assessing vocal cord function.

ENDOSCOPY

Direct Laryngoscopy

Direct visualization of larynx by means of a laryngoscope will help to assess the lesion, note its extent, and vocal cord movement. Biopsies and excision of benign lesions of the larynx can be done through the laryngoscope.

Flexible Nasopharyngolaryngoscopy

This procedure gives an excellent view of the larynx and laryngopharynx and this can be performed as an outpatient. It also helps to demonstrate the lesion to others and for taking still or video pictures.

Microlaryngoscopy

Direct laryngoscopy in conjunction with the use of an operating microscope helps to magnify laryngeal lesions, to perform precise surgery of larynx, accurate laser therapy and to take still and video photography.

Nasal Endoscopy

Examination of the nasal cavities using an endoscope has become an integral part of investigation of diseases of nose and paranasal sinuses (Figs 53.25 to 53.28).

Indications

1. Chronic and recurrent sinusitis
2. Headache and facial neuralgia
3. Permanent coryza
4. Epistaxis, epiphora, chronic pharyngitis and laryngitis, and chronic otitis media
5. Disease of epipharynx
6. Hyposmia/anosmia
7. CSF rhinorrhea
8. For biopsy from nose and paranasal sinuses.

Procedure

The examination is carried out with the patient seated or recumbent. The nasal cavity is anesthetized by administering local anesthetic spray or inserting swabs soaked with local anesthetic. The instruments used are 0°, 30° and 70° scopes, which are 4 mm in diameter for adults and 2.7 mm in diameter for infants.

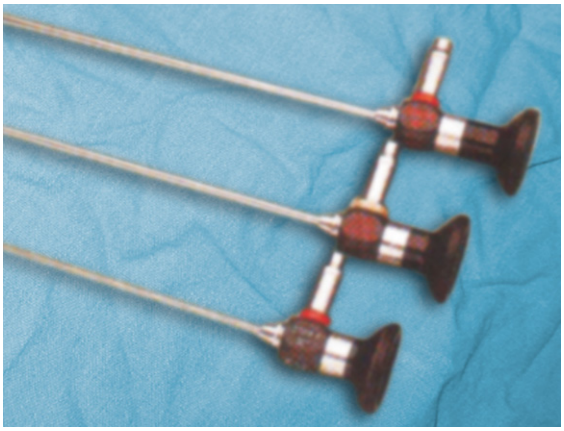


Fig. 53.25: Nasal endoscopes

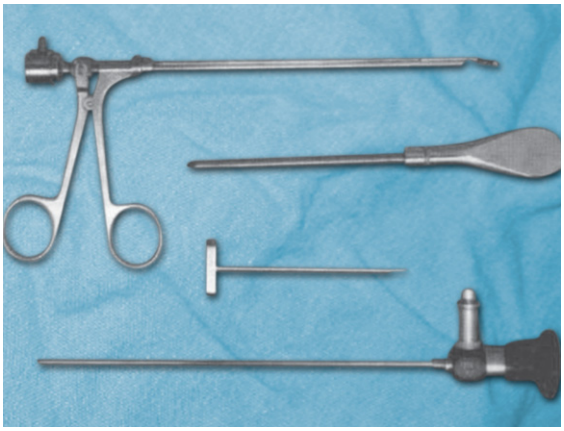


Fig. 53.27: Instruments of sinus endoscopy

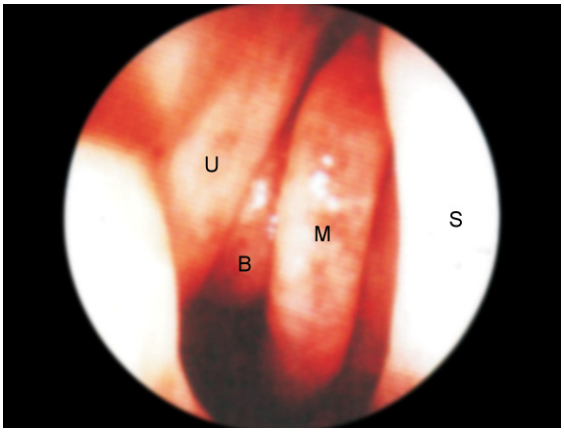


Fig. 53.26: Endoscopic view of nasal cavity. U–uncinate process, B–bulla ethmoidalis, M–middle turbinate, S–septum nose

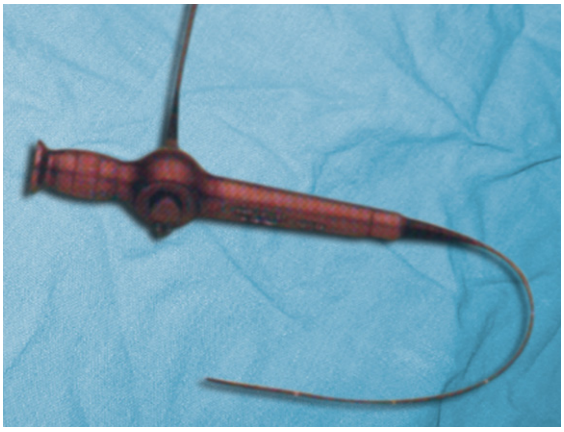


Fig. 53.28: Flexible nasopharyngoscope

In the first pass the 0° scope is advanced along the floor of nose, inspecting the inferior meatus, inferior turbinate and nasal septum till the posterior choana is reached. The eustachian tube's orifice and the nasopharynx are visualized and the scope is withdrawn. The second pass is along the middle meatus visualizing the middle turbinate and the middle meatus. This scope is advanced right up to the anterior wall of sphenoid sinus visualizing its ostium. Any pathology in the nostril and nasoparynx can be visualized clearly by nasal endoscopy.

The *30° scope* is useful to visualize the nasal ostium of nasolacrimal duct and the spheno-ethmoidal recess.

The *70° scope* is useful in assessing the entire middle meatus and the olfactory fissure.

Sinus Endoscopy

Maxillary sinus endoscopy is useful in the diagnosis of tumors, fungal diseases and chronic maxillary sinusitis. It can be performed either via the canine fossa or transnasally via supraturbinal window or infraturbinal window (Fig. 53.27).

Nasopharyngoscopy

This can be performed either with a rigid nasopharyngoscope or a flexible nasopharyngoscope. Very early lesions of nasopharynx can be visualized and biopsied for diagnosis (Fig. 53.28).

Diagnostic Antral Puncture

This procedure helps to confirm the diagnosis of chronic maxillary sinusitis and for taking wash-outs

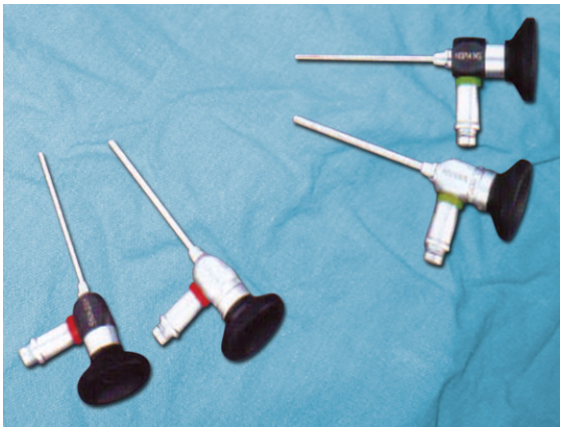


Fig. 53.29: Otoendoscopes

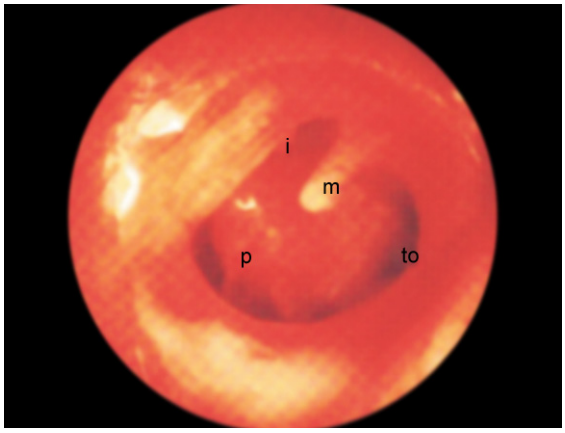


Fig. 53.31: Tympanic membrane perforation seen through otoscope

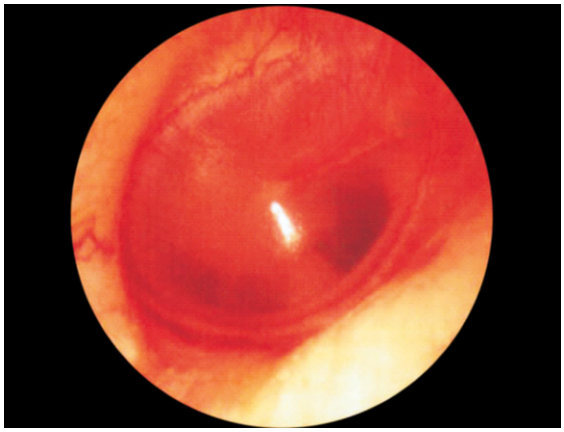


Fig. 53.30: Normal tympanic membrane seen through otoscope

from the antrum for microbiological tests and exfoliative cytology for malignant cells. Contrast radiography of the sinuses can be done after antral puncture.

Otoendoscopy (Figs 53.29 to 53.31)

Advantages of otoendoscopy are:

1. Assessment of the entire tympanic membrane, the annulus and the wall of the auditory meatus.
2. Helps in the differential diagnosis of fixed and mobile retraction of the tympanic membrane, examination of the recesses, adhesive processes, atelectasis, cholesteatomas and others.
3. Assessment of ossicular chain in cases of tympanic membrane perforation
4. View into the tympanomeatal angle
5. Assessment of radical mastoid cavity
6. Postoperative examination
7. Photographic and video documentation.

0° and 30° endoscopes with 3 mm and 6 mm diameter are available.

POLYSOMNOGRAPHY

This study is performed in a sleep laboratory in order to confirm the diagnosis of sleep apnea syndrome and to assess its severity. It involves the continuous recording of EEG, ECG electrooculogram, chin electromyogram and respiratory movements of the chest and abdominal wall throughout sleep. Oronasal air flow and oxygen saturation are monitored. In addition to the detection of oxygen desaturation and cardiac arrhythmias, these recordings also allow sleep to be staged, REM sleep to be recognized and obstructive central and mixed apneas to be distinguished.

SECTION

19

Examination of Oral Mucosa and Teeth (Dental Examination)

CHAPTER

54 Oral Mucosa, Teeth and Gums

Angel Jacob

Examination of oral mucosa, Teeth and gums, Salivary glands, Ulcers of oral mucosa, Lumps or swelling in the mouth, Xerostomia, Halitosis, Examination of the teeth, Mandibular fracture and dislocation, Malocclusion of teeth, Examination of gingival and periodontium, Bleeding from the gums gingival enlargement

EXAMINATION OF THE ORAL MUCOSA, TEETH AND GUMS

The basic instruments for oral examination are—mouth mirror, graduated probe, explorer and tweezer (Fig. 54.1).

The examination may be carried out in this order—buccal lining mucosa, tongue, floor of the mouth and the ventral surface of the tongue, hard and soft palate, throat, salivary glands, salivary flow, gingiva, teeth.

An orderly examination of the oral mucosa should be done making the patient sit in an upright position.

Upper and Lower Labial Sulci

Retract the lips with two mouth mirrors.



Fig. 54.1: Mouth mirror, graduated probe, explorer and tweezers

Cheek Mucosa (Fig. 54.2)

With the mouth wide open retract the cheek.

Upper and Lower Buccal Sulci

Retract the cheek with the mouth half open (Fig. 54.3). Repeat the same procedure on the other cheek and upper and lower buccal sulci.

Dorsum: Inspection should be performed at rest and on protrusion. Look for reduced mobility (Fig. 54.4).

Tongue

Examination of the Lateral Border

The tip of the tongue can be held with a guaze and moved to one side. The cheek should be retracted and the lateral borders of the tongue viewed. This should be repeated for the other side (Fig. 54.5).

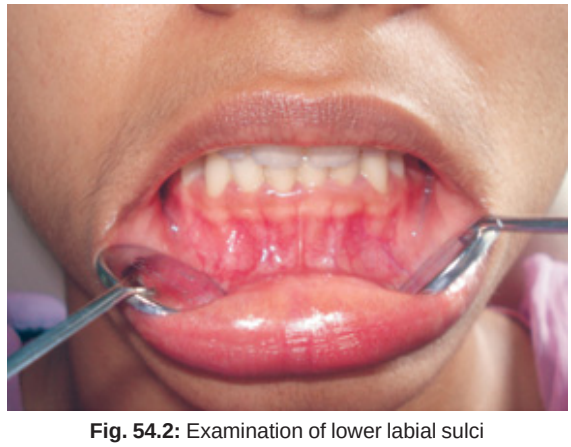


Fig. 54.2: Examination of lower labial sulci



Fig. 54.3: Examination of the upper and lower buccal sulci



Fig. 54.5: Examination of the lateral border of the tongue



Fig. 54.4: Examination of the dorsum of the tongue



Fig. 54.6: Examination of the floor of the mouth

Floor of the Mouth

Can be viewed with the tip of the tongue raised to touch the palate (Fig. 54.6). Ventral surface of the tongue can also be viewed by asking the patients to raise the tongue and touch the palate.

Palate

Tongue should be depressed with a spatula and visual examination and palpation of the hard palate can be done.

Soft Palate

Can be visually examined and its mobility assessed by requesting the patient to say "Ah" (Fig. 54.7).

Throat

The tongue can be depressed again using a tongue spatula. Request the patient to repeat "Ah" and the pillars of the fauces, tonsils, uvula and oropharynx can be viewed.



Fig. 54.7: Examination of the soft palate

Salivary Glands

Parotid Salivary Glands

The lower part of the ear lobe may be turned outward if the gland is swollen. Palpate the gland for enlargement and tenderness. The gland is located mainly distal to the ascending ramus of the mandible. A better view may be obtained if the

gland can be viewed from the back. The opening of the Wharton's duct of the parotid salivary gland must be examined for inflammation. It is present opposite upper second molar tooth.

Submandibular Salivary Glands

Index and middle finger of one hand is used intraorally and the same fingers of the other hand extraorally. Palpate the gland above and below the mylohyoid and examine the ducts of the gland for calculi and the opening for signs of inflammation. Bimanual palpation of the submandibular glands and ducts should be done to detect enlargement, tenderness or calculi.

Sublingual salivary gland duct opening can be examined on the ventral surface of the tongue for inflammation or other abnormalities.

Temporomandibular joint can be examined for range of movement, tenderness, sounds, locking. Note for limitation of mouth opening and deviation to one side. Bimanual palpation is done by pressing over the lateral aspect of the joint. Intra-auricular palpation is done by placing the little finger into the external auditory meatus and gently pressing forward can reveal tenderness. Clicking sounds can also be heard on opening due to the sudden movement of the disk relative to the condyle. TMJ locking and dislocation can also be present.

Lining Mucosa

Normal buccal mucosa has the following features:
- Linea alba buccalis
- Fordyces granules
- Wharton's duct.

Inspection reveals the site, size and shape and palpation reveals whether the lesion is soft, firm or hard. Note whether the edges are well defined or diffuse and if the lesion is mobile or fixed.

The following changes can be observed in the oral mucosa:

Ulcers, white patches, red, vesicular and bullous lesions, enlargements and swellings. Oral changes in systemic diseases, and miscellaneous conditions.

ULCERS OF ORAL MUCOSA

Traumatic

Over extended denture, sharp tooth, sharp edge of a fractured tooth, thermal burns, chemical burns, iatrogenic.

Infective

Bacterial—tuberculosis, acute necrotizing ulcerative gingivitis, syphilis. Viral—herpes simplex, herpes zoster, measles, cytomegalovirus, coxsackievirus, human immunodeficiency virus, human herpes virus-8.

Fungal—histoplasmosis, mucormycosis, aspergillosis, cryptococcosis, blastomycosis, candidiasis.

Neoplastic

Squamous cell carcinoma, Non-Hodgkin's lymphoma, Kaposi's sarcoma (human herpes virus-8).

Malignant melanoma, malignant salivary gland tumors.

Systemic

Lichen planus, pemphigus, mucous membrane pemphigoid, erythema multiforme, hematologic disorders like (anemia, neutropenia, leukemia, immunosuppression, e.g. AIDS), systemic lupus erythematosus, gastrointestinal disorders like Chron's disease, ulcerative colitis.

Miscellaneous

Recurrent aphthous stomatitis, ulcers due to allergic reaction, necrotizing sialometaplasia, Behcet's syndrome and lichenoid reactions.

An ulcer should be examined using a systematic approach.

Site

Adjacent to a sharp tooth, edges of denture—traumatic.

Interdental papilla: Acute necrotizing ulcerative stomatitis.

Posterior part of the mouth: Coxsackievirus, e.g. herpangina.

Number of ulcers: Multiple sites suggest viral infection or recurrent aphthae.

Shape

Round, oval, crescentic—traumatic ulcer, irregular—cytomegalovirus, coalescing—herpetic ulcers.

Angular or stellate—TB, punched out—tertiary syphilis.

Floor

Should be examined for color.

Bleeding and raw—pemphigus, erythema multiforme, bullous pemphigoid, traumatic ulcer.

Yellow floor—aphthous ulcer.

Slough: Pseudomembranous slough—acute necrotizing ulcerative gingivitis.

Fungating and scab formation—Granulation.

Base

Induration present or absent: Induration is suggestive of malignancy.

Edge

Raised, rolled or everted: Malignant ulcers.

Undermined/overhanging: TB ulcers.

Punched out: Tertiary syphilitic ulcers.

There may be associated problems like secondary infection and pain in inflammatory diseases. Ulcers are painless in early stages of malignancy. There may be reactive lymphadenopathy that may inhibit eating and speech.

The most common oral ulcers are described below.

Traumatic Ulcer

On inspection: The site of the ulcer will be adjacent to a carious tooth, broken denture, periphery of a denture or an orthodontic appliance. They are usually single, variable in size, oval, round, crescentic or elliptical in shape, flat or slightly depressed. The margins are red and there will be serosanguineous or serofibrineous exudates. A raw red tissue base is revealed when the necrotic slough is removed.

On Palpation

There is no induration and the ulcer heals within a few days of removal of the trauma. There is painful regional lymphadenopathy.

Differential Diagnosis

Primary syphilitic lesions, tubercular lesions, necrotizing sialometaplasia, dystrophic ulcer.

Lab Investigation

If the ulcer does not heal after a few days of removal of the trauma, a biopsy should be taken suspecting squamous cell carcinoma.

Tuberculous Ulcer

Inspection shows irregular lesion with ragged undermined borders with a yellowish granular base. The mucosa surrounding the ulcer is inflamed and edematous. On palpation, there is only minimum induration.

Investigations

Biopsy, chest radiography, microbiological tests for tubercle bacilli, sputum analysis.

Syphilitic Ulcer

On inspection, chancre of primary syphilis has narrow copper colored, slightly raised borders with reddish brown base at the center. It measures around 0.5 to 2 cm in diameter. It is painful due to secondary infection and covered with a grayish white film. Found on lips, gingiva, oral mucosa lateral surface of the tongue, soft palate, tonsillar and pharyngeal region.

Palpation of the lymph node reveals regional lymphadenopathy.

Secondary Syphilis

On inspection, they appear as slightly raised grayish white lesions surrounded by an erythematous base covered by grayish white membrane. Found on the tongue, buccal mucosa, tonsillar and pharyngeal region. These are the mucous patches of secondary syphilis. Confluence and coalescence of these mucous patches give rise to snail track ulcers. Raised papular lesion developed at the commissure of the lip and a fissure separating the upper lip portion from the lower lip portion is the split papule. Flat silver gray wart like papule, sometimes having ulcerated surface and painless is the condyloma latum. Regional lymphadenopathy is usually present.

Tertiary Syphilis

Punched out ulcer with vertical walls and red granulomatous base is the gumma in tertiary syphilis. It is usually found on the palate, tonsils and tongue.

Investigations

Smear from the surface of the chancre, serological tests.

Koplik's Spots

On inspection, they are seen as small, white spots on a red base on the buccal mucosa near the molar teeth in measles preceding the rash. They resolve after 3 to 4 days and are replaced by red maculopapular generalized skin rash.

Ulcers Associated with Allergic Reactions

On inspection, the lesions are diffuse in distribution. It varies in appearance from multiple areas of erythema, erosion or ulceration. In the early stages of reaction, vesicles or bullae may appear on the mucosa. Purpuric spots and angioneurotic edema may also be seen. The gingiva may also show ulceration or necrosis.

Differential Diagnosis

Recurrent herpes simplex infection, major apthae, acute necrotizing ulcerative gingivitis, pemphigus, mucous membrane pemphigus or erythema multiforme.

Acute Necrotizing Ulcerative Gingivitis

Inspection shows punched out crater like depressions on the interdental papilla and marginal gingiva. There is a pseudomembranous slough covering the ulcer and its removal reveals a raw surface.

This is associated with sudden onset of pain, tenderness, profuse salivation, metallic taste, fetid odor and usually appears in immunocompromised patients, debilitated patients, starvation, smokers and people with protracted work without adequate rest.

Differential Diagnosis

Pemphigus, bullous pemphigoid, herpetic gingivostomatitis, cyclic neutropenia, erythema multiforme, herpangina and erosive lichen planus.

Investigations

Microbiological analysis, biopsy and histopathological examination.

Aphthous Stomatitis

Inspection shows single or multiple superficial erosions covered by a grayish membrane. There is localized edema that forms small white papules within hours that ulcerate and gradually enlarge over the next 72 hours. Minor aphthae are small 0.3 to 1cm and heals without scarring (Fig. 54.8). Major aphthae are large 1 to 5 cm and heals with scarring. Herpetiform ulcers are multiple shallow ulcers that are pin head shaped that can coalesce. They are more painful compared to their size.

Differential Diagnosis

Traumatic ulcer.

Pemphigus

Inspection reveals bullae which rapidly form shallow ulcers. The epithelium can be peeled off easily leaving behind a denuded base. This is known as Nicolsky's sign. The margins are ragged, the surface covered with white or blood tinged exudates (Fig. 54.9). The gingiva is diffuse and erythematous.



Fig. 54.8: Aphthous ulcer (arrow)

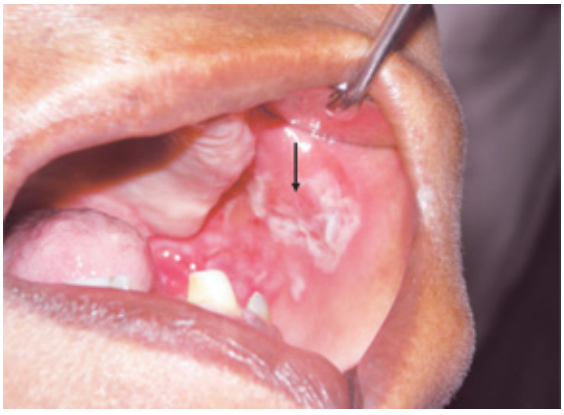


Fig. 54.9: Pemphigus (arrow)

On palpation the lesion bleeds easily and there is severe pain.

Differential Diagnosis

Recurrent aphthous stomatitis, erythema multiforme, bullous drug induced exanthematous lesions, bullous mucous membrane pemphigoid. About 90% of pemphigus also appears in the oral mucosa and 60% of it appears first in the oral mucosa.

Investigations

Nikolsky's sign, biopsy, immunofluorescent antibody test.

Erythema Multiforme

Inspection: Usually appears on the lips followed by buccal mucosa, palate, tongue and face. It appears as vesicles that rapidly turn into ulcers. The base is erythematous. Patients cannot swallow and saliva drools out and is blood tinged. The lips are extensively involved and oral mucosa is denuded of epithelium in large areas. Sloughing of mucosa reveals bright red raw surface (Figs 54.10 and 54.11).

Differential Diagnosis

Primary herpetic gingivostomatitis, pemphigus vulgaris, mucous membrane pemphigoid, allergic reactions, and erosive lichen planus.

Investigation

Mucosal biopsy.

Erosive Lichen Planus

Seventy percent of patients with skin involvement has oral lesions but only 10% of patients having oral lesions have skin lesions. It is seen in women over 30 years of age. On inspection, they are painful ulcers that are shallow, irregular erosions. They are bilateral and affects the buccal mucosa, tongue, labial mucosa and gingiva. The palate and lingual mucosa are usually spared. The size ranges from a few millimeters to several centimeters in diameter. The floor is yellow with a layer of fibrin covering the base and the edges may have sunken margins due to fibrosis and the borders are usually erythematous.

Differential Diagnosis

Gingival atropic lesions resemble mucous membrane pemphigoid.

Investigation

Mucosal biopsy.

Bullous Pemphigoid

The initial defect is subepthelial in the lamina lucida portion of the basement membrane.

Inspection

There are presence of bullous lesions initially which rupture to form ulcerations and erosions. The gingiva presents with inflammation, generalized edema, desquamation and localized areas of vesicle formation. The vesicles may also be present on the

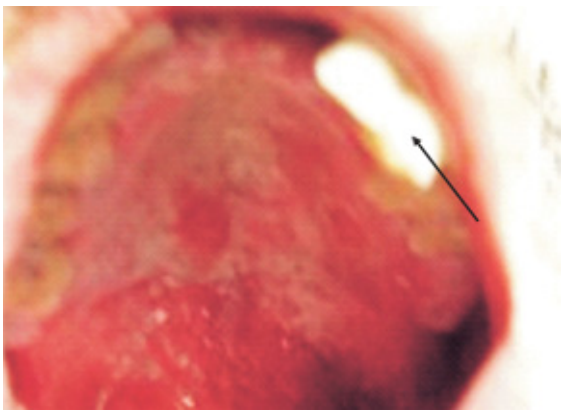


Fig. 54.10: Erythema multiforme on palate (arrow)



Fig. 54.11: Erythema multiforme on lips (arrow)

buccal mucosa, floor of the mouth, palate and tongue.

Differential Diagnosis

Pemphigus, bullous mucous membrane pemphigoid.

Laboratory Tests

Indirect immunofluorescence antibody test demonstrates circulating IgG antibodies against basement membrane.

Bullous Mucous Membrane Pemphigoid

The mouth may be the only site involved. On inspection the lesions are vesiculobullous and they are thick walled so they persist for a longer time than the other lesions (around 24 to 48 hours). The ruptured vesicle leads to a raw bleeding ulcer surrounded by a zone of erythema. The gingiva is edematous and red.

Laboratory Investigation

Direct immunofluorescent study will show fluorescent immunoglobins and complements in the basement membrane zone.

Differential Diagnosis

Pemphigus vulgaris, erythema multiforme, bullous pemphigoid, Behcet's syndrome.

Behcet's Syndrome

Multisystem disorder with common triad of features that include ulcers of the aphthous type, genital ulceration and eye lesions.

Necrotizing Sialometaplasia

A painful ulcer on the palate found midway between the palatal raphe and the gingival margin usually in the molar region. On inspection they are single and large up to two centimeters in diameter. The margins are irregular in shape with the base often being the palatal bone and the floor is yellow with necrotic debris. The edges are inverted or heaped-up and on palpation the ulcer is indurated. This resembles squamous cell carcinoma clinically and histopathologically also resembles squamous cell carcinoma and mucoepidermoid carcinoma but the condition is self-limiting and heals spontaneously in 2 to 3 months.

Crohn's Disease

Inspection reveals recurrent oral aphthae with diffuse swelling of the lips, cheeks and gingiva. There is hyperplasia of the mucosa, giving rise to mucosal tags or a cobble stone appearance, erythematous hyperplastic gingivitis and large, linear ulcers that are ragged are typically seen in the vestibular region.

Investigations

Biopsy and hematological tests.

Leukemia

Oral manifestations may be the initial complains in acute leukemias and can be present in up to 90% of the cases. Inspection shows swollen, spontaneously bleeding gums, gingival swelling, painful ulcers, petechia, ecchymosis, hemorrhage and mucosal pallor.

Investigation

Blood examination.

MALIGNANT ULCERS

Squamous Cell Carcinoma

The oral mucosa is a very common site for malignancy in India. The habits of "Pan" chewing and tobacco smoking predispose to the development of oral cancer. On inspection the lesion appears as circular, crescentic or irregular ulcers with raised, everted or rolled edge. The floor may be granular and ragged and bleed easily with the base indurated and fixed to the deeper tissues. The site is often the tongue, floor of the mouth, buccal mucosa and alveolar ridge (Figs 54.12 to 54.14). The lesion may be painless in the early stages but may become painful when the tumor invades the neural tissue. There are swollen nontender glands in the neck. There is loosening of the teeth in carcinoma of the gingiva.

Investigations

Biopsy and histopathological examination, plain radiology, CT, MRI and bone scintigraphy.

Non-Hodgkin's Lymphoma

Inspection reveals a circular or irregular ulcer on the gingiva, palate, buccal mucosa or pharynx. The

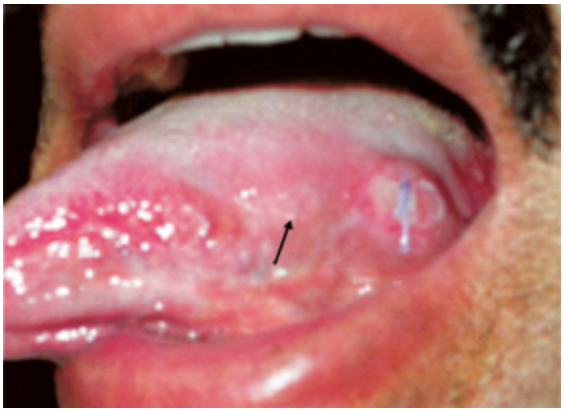


Fig. 54.12: Carcinoma tongue early stage (arrow)



Fig. 54.13: Carcinoma tongue late stage (arrow)

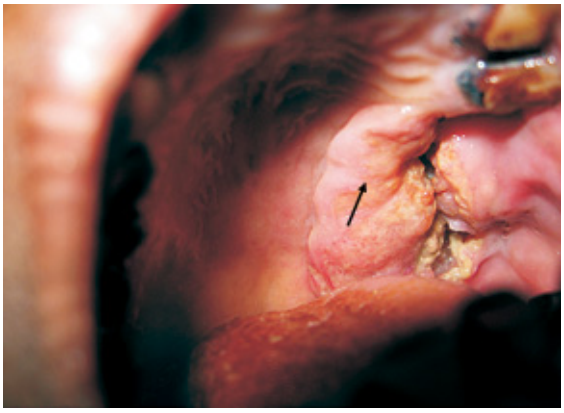


Fig. 54.14: Carcinoma alveolar ridge (arrow)

floor is yellow and may bleed due to trauma. The margins are red and inflamed. There is cervical lymphadenopathy and trismus when masticatory muscles are involved or facial swelling when buccal sulcus is involved. There can also be tooth mobility or loss and oroantral communications due to extensive alveolar bone destruction.

Diagnostic Tests

Biopsy and histopathological examination, immuno chemical analysis and radiological examination.

Malignant Salivary Gland Tumors

On inspection it can present as a painless swelling of the palate. It may also appear as an ulcer that is painful. The size can extend to several centimeters.

Investigations

Biopsy and histopathological examination, CT scanning and MRI.

Kaposi's Sarcoma

On examination, they appear as typically single or multiple blue, red or purple, macules, papules, nodules or ulcers. It begins as flat, blue, red or purple macules. As the lesion increases in size they become nodular and raised similar in clinical appearance to hemangiomas or ecchymosis. The size is variable from a few millimeters to several centimeters. Advanced lesion may show a central area of ulceration. Floor of the ulcer is gray, necrotic and may bleed. Early lesion is painless but advanced lesion is painful. Edges are red with no induration. The most common site is the palate opposite the second molar tooth. Kaposi's sarcoma is most common in AIDS patients.

Kaposi's sarcoma can also occur in other non-HIV related immunosuppressive states such as patients on long-term cyclosporine therapy.

Investigations

Biopsy and histopathological examination, HIV antibody test.

Differential Diagnosis

Hemangiomas, ecchymosis.

Malignant Melanoma

Inspection shows ulcer with irregular outline that is black, brown or red in color found in the hard palate, maxillary gingiva or alveolar ridge. The size ranges from a few millimeters to more than a centimeter in diameter. Bleeding may be present in the later stages. Any hyperpigmented melanotic oral

lesion with irregular margins or a history of growth should be treated with utmost suspicion and early biopsy.

Investigations

Biopsy and histopathological examination.

Painful ulcers	*Painless ulcers*
Traumatic	Syphilitic ulcer
TB ulcer	Squamous cell carcinoma
ANUG (Acute necrotizing ulcerative gingivitis)	Kaposis sarcoma
1º herpetic gingivosto-matitis	Non-Hodgkin's lymphoma
Herpes zoster	Malignant melanoma
Cytomegalovirus	Malignant salivary gland tumors
Herpangina	
Hand, foot and mouth disease	
Fungal infections	
Mucous membrane pemphigoid	
Pemphigus	
Erythema multiforme	
Erosive lichen planus	
Behcet's syndrome	
Necrotizing sialometaplasia	
Recurrent aphthous stomatitis	
Aphthous ulcers	

KERATOTIC AND NON-KERATOTIC WHITE LESIONS

Normal variation:
- Leukoedema
- Fordyce granule
- Linea alba.

Fordyce Granules

Inspection shows small, yellowish spots either discretely separated or forming relatively large plaques projecting above the surface. On the tongue they appear as dome shaped nodules varying from a few mm to 2 cm in diameter on the midline dorsum of the tongue. They are sharply delineated with a smooth surface. They do not ulcerate. On palpation the lesions have a slightly cheesy consistency.

Linea alba is a white line on the buccal mucosa seen at the line of occlusion.

Removable White Patch

Leukoedema (variant of oral mucosa that disappears on stretching).
- Epithelial or food debris
- Milk curd (babies)
- Chemical trauma
- Pseudomembranous candidiasis.

Nonremovable White Patches

a. Congenital
 - White spongy nevus
 - Dyskeratosis follicularis

b. Acquired

Traumatic

Frictional keratosis
Submucous fibrosis
Smoker's keratosis (Fig. 54.15).

Infective

Candidal leukoplakia (chronic hyperplastic candidiasis, pseudomembranous candidiasis)
Oral hairy leukoplakia
Syphilitic leukoplakia.

Dermatological

Lichen planus and lichenoid reactions (Fig. 54.16)
Systemic lupus erythematosus
Discoid lupus erythematosus.

Neoplasia and Premalignant Conditions

Leukoplakia (Fig. 54.17)
Speckled leukoplakia
Erythroplakia
Squamous cell carcinoma
Oral submucous fibrosis.

Miscellaneous

Vitamin A deficiency
Skin graft.



Fig. 54.15: Smoker's keratosis



Fig. 54.16: Lichen planus



Fig. 54.17: Leukoplakia

Many conditions are present in the mouth that may or may not be malignant. When the etiology is unclear, a biopsy should always be carried out for accurate diagnosis. A detailed and careful history regarding the duration of the lesion, pain, history of frictional trauma, chemical burns, smoking and chewing tobacco, alcohol and a comprehensive medical and family history should be taken.

LUMPS OR SWELLING IN THE MOUTH

Normal
- Unerupted teeth
- Pterygoid hamulus
- Parotid papillae
- Foliate papillae

Developmental
- Lymphangioma
- Hemangioma
- Maxillary and mandibular tori
- Hereditary gingival fibromatosis
- von Recklinghausen's neurofibromatosis

Traumatic
- Epulis
- Epithelial polyp
- Hematoma
- Denture granulomas

Inflammatory
- Abscess
- Pyogenic granuloma
- Infections
- Insect bites
- Crohn's disease
- Sarcoidosis
- Wegener's granulomatosis

Cystic
- Eruption cyst
- Developmental cysts
- Cysts of infective origin
- Hormonal
- Pregnancy gingivitis
- Oral contraceptives

Drugs
- Phenytoin
- Cyclosporin
- Calcium channel blockers

Blood dyscrasias
- Leukemia
- Lymphoma
- Benign neoplasm
- Malignant neoplasm

Others
- Angioedema
- Amyloidosis
- Other deposit.

XEROSTOMIA

Patient complains of dry mouth alone or combination with other clinical features such as dryness of the eyes and other mucosae (nasal, laryngeal and genital), with other eye complaints (inability to cry, blurring, light intolerance, burning, itching and voice changes). There is difficulty in swallowing and eating dry food like biscuits, difficulty in controlling dentures in speech and swallowing, mouth soreness, unpleasant taste or loss of taste,

saliva not expressible from the parotid gland, characteristic lobulated tongue, red with partial or complete depapillation. There may be complications of xerostomia like dental caries and candidiasis. There can also be ascending suppurative sialadenitis.

HALITOSIS (OFFENSIVE BREATH)

Diagnosis of halitosis is made from full history, examination or assessment of halitosis simply by smelling the exhaled air (organoleptic method), halimeter which give the amount of volatile amines, sulphur compounds, methylmercaptans and others in the breath.

If there is no genuine halitosis it is due to psychogenic causes. Halitosis can be caused due to recently ingested food like garlic, onion, drugs like alcohol, chloral nitrites/nitrates, dimethyl sulphoxide, cytotoxics, phenothiazines, amphetamines or smoking. It is also caused by oral, sinus or pharyngeal infections like abscess, dry socket, pericoronitis, acute ulcerative gingivitis, tonsillitis, sinusitis nasal discharge or foreign body and due to dry mouth or respiratory disease, hepatic disease, renal disease, gastrointestinal disease, diabetes mellitus or other conditions.

EXAMINATION OF THE TEETH

Examination of the tooth is done by using a mouth mirror and an explorer. Dental caries may be present in the pits on fissures on the biting surface of the teeth, on the smooth surface below the contact point between the teeth and also present on root surface. It can be detected on inspection by using a mouth mirror and a probe. If there is a catch on pulling the explorer over the tooth surface, then dental caries is suspected (Fig. 54.18).

Teeth are opaque white in color if the enamel, dentine and the pulp are intact. Attrition of the teeth and decrease in the amount of enamel present on the teeth will expose the underlying dentine giving it a yellow discoloration. There is increase in sensitivity. Caries can present with varied symptoms like no symptoms in initial lesion, sensitivity, sharp shooting, intermittent pain and continuous pain that interferes with sleep in case of infection of the pulp and periodontal tissues. There will also be referred pain to the shoulder and neck in case of mandibular molar teeth, orbital region in case of canines, maxillary sinus region and temporal region in case of maxillary molars. Presence of a periapical abscess as a result of caries can also be detected by percussion of the tooth with a handle of an instrument (Fig. 54.19). Presence of pain indicates periapical lesion which can even be excruciating.

Sharp stabbing pain is associated with exposed dentine associated with caries, fractured restoration, fractured tooth, cracked tooth, early pulpitis, trigeminal neuralgia and glossopharyngeal neuralgia.

Dull Throbbing Pain

- Late pulpitis
- Apical and lateral periodontitis
- Periodontal-endodontal lesion
- Acute necrotising ulcerative gingivitis
- Dry socket



Fig. 54.18: Detecting dental caries



Fig. 54.19: Percussion of tooth

- Periodic migrainous neuralgia
- Herpes zoster
- Giant cell arteritis
- Tumors
- Sinusitis
- Temporomandibular joint (TMJ) disorders
- Atypical odontalgia
- Atypical facial pain.

Burning Pain

- Burning mouth syndrome
- Post herpetic neuralgia
- Ramsay Hunt syndrome (geniculate herpes)
- Pain arising from pathology is usually unilateral
- Bilateral pain crossing the midline and if it occurs in the maxillary teeth region—sinusitis
- Excruciating pain on the merest contact with a trigger zone on the face suggests trigeminal neuralgia. Similar pain on swallowing suggests glossopharyngeal neuralgia.

Dental Pain

- Differential diagnosis:
- Pulpal pain
- Periodontal pain
- Gingival pain
- Pain related to bone
- Pain associated with denture bases.

Pain on biting or touching a tooth may indicate acute periodontitis or pericoronitis. Pain on hot or cold stimulation suggests exposure of root or coronal dentine dental caries, defective restoration, fractured tooth or pulpitis. Pain with sweet food suggests exposure of root or coronal dentine (dentinal hypersensitivity) or caries. Intermittent pain on biting, particularly on release of pressure suggests a cracked tooth.

Dental caries involving the enamel and dentine alone will present with sensitivity sometimes mimicking pain which is sharp stabbing pain. There will be pain on intake of hot, cold or sweet food. The pain is relieved on removal of the stimulus. The pain can be localized to the involved tooth. Percussion of the tooth with the handle of the probe will not produce pain.

Investigation—Radiograph of the tooth.

Differential Diagnosis

Faulty restoration, cracked tooth, broken restorations, abrasions, attritions and erosions of teeth, gingival recession.

Diagnostic Tests

1. Tooth can be identified using cold air or ethyl chloride after isolating individual tooth.

 When the caries involves the pulp there will be unilateral, stabbing pain recognized as a tooth ache. Pain may be intermittent and immediate in onset to hot, cold and sweet stimuli. Responds more to cold than hot stimuli which lasts for a short duration around 15 seconds after the stimulus has been removed. The pain is poorly localized. Inspection shows large carious lesion involving the pulp or a large intracoronal or extracoronal restoration with secondary caries. (Fig. 54.20).
2. Exaggerated response to cold, heat and sweet stimuli. Intraoral periapical radiograph.

 When the pulpitis is acute there is unilateral sharp stabbing pain, becoming dull or throbbing with time, exaggerated response to stimuli, there will be referred pain to the shoulder, neck, orbital region, temporal area. Cold may relieve pain by reducing pressure. Inspection shows a large carious lesion.
3. Tooth becomes tender to percussion. Intraoral periapical radiographs. When pulpitis is chronic



Fig. 54.20: Dental caries

there is intermittent mild pain over a long period and the pain is poorly localized.

When the pulpal involvement extends to the periodontal ligament there is unilateral severe, continuous pain and the tooth is exquisitely tender to touch. It is localized and the pain is a severe enough to prevent eating and sleeping. Inspection will reveal a large carious lesion or large restoration. Swelling appears and an abscess may point at the apical region of the tooth. The surrounding gingival tissues will be inflamed. If drainage of pus through the gingival crevice, there is presence of a periodontal pocket. Regional lymph nodes will be enlarged and tender and tooth discolored. There will be a soft tissue swelling at the apices labially or lingually and or a sinus may be present. The tooth will be mobile and extruded.

4. Pain on percussion, intraoral periapical radiograph and vitality tests. Distinguishing pain of dental origin from maxillary sinusitis. Proper history has to be taken. In case of maxillary sinusitis, pain cannot be localized to a single tooth, pain on bending the head and a history of rhinitis. Vitality tests will show that the tooth is vital. In pain is of dental origin, pain can be localized to the particular tooth and the vitality tests will show if the pulp is hyperemic or necrotic.

Investigations: Intraoral periapical radiograph, radiograph of the maxillary sinus and CT scan.

Mandibular Fracture

Intraoral examination elicits swelling, ecchymosis and abnormal mobility of bone. The occlusion should be checked for any derangement, including anterior open bite. The teeth have to be examined for mobility and fracture. Alveolar fracture is suspected when several teeth are moving simultaneously.

Mandibular Dislocation

This presents with symptoms of pain and inability to close the mouth. On inspection the mouth is wide opened and fixed in the position. There is pain on palpation of the muscles of mastication and the condyles. The condyles will be palpable anterior to the articular eminence. There will be dribbling and pooling of saliva due to difficulty in swallowing.

Malocclusion of teeth: Angle defined occlusion as the normal relation of the occlusal individual planes of teeth when the jaws are closed. Occlusion is a complex phenomenon involving the teeth, periodontal ligament, temporomandibular joint, muscles, jaws and the masticatory system. Malocclusion may be due to dental, skeletal or a combination of causes. Dental irregularities are due to crowing, spacing, crossbite, open bite and deep bite (Fig. 54.21). Malocclusion due to irregularities of the teeth can be corrected by orthodontic therapy (Fig. 54.22), Skeletal malocclusion if noticed during the growth period can be corrected by growth modification



Fig. 54.21: Before orthodontic treatment



Fig. 54.22: After orthodontic treatment

procedures like functional and orthopedic appliances. After the growth is completed, skeletal malocclusions are corrected by means of orthognathic surgery.

EXAMINATION OF GINGIVA AND PERIODONTIUM

The healthy gingiva is pale pink or coral pink in color with the marginal gingiva scalloped at the level of cementoenamel junction. The interdental papilla fills the embrasures between the teeth. There is presence of stippling in the attached gingiva region of the interdental papilla (Fig. 54.23).

Changes in the Gingiva due to Disease

In the gingiva, there may be changes in the color, contour, consistency, texture, tendency to bleed, suppuration and pain. There can be the presence of vesicular, bullous and ulcerative lesions, red and white lesions, pigmented lesions, benign and malignant lesions. There can also be presence of plaques, papules, macules, pustules, sinuses and fistulas. The gingiva should be inspected for its color, contour, consistency, surface texture, size, position, tendency to bleed and pain. Palpate the lateral and apical areas of the tooth. This may help to locate the origin of any radiating pain that the patient cannot localize. Infection deep in the periodontal tissues and the early stages of periodontal disease can also be located by palpation. Presence of pus in the periodontal tissues as it occurs in periodontal infection can be determined by placing the ball of the index finger along the lateral aspect of the marginal gingiva and applying pressure in a rolling motion towards the crown (Fig. 54.24).

The gingiva should be probed with a graduated probe (William's graduated probe) to detect the presence of pockets (Fig. 54.25). The presence of periodontal pocket is a sign of periodontitis.

Periodontitis can be diagnosed by the presence of periodontal pockets, pus discharge, mobility, pathological migration of teeth, periodontal abscess, pain and bleeding. Since periodontitis is a chronic infection releasing large amounts of cytokines into the blood stream, it is considered to be risk factor for coronary heart disease, preterm low birth weight infants, cerebrovascular accidents, poor glycemic control in diabetics and risk of pneumonia.

In some situations gingiva, buccal mucosa and tongue may be the only sites at which systemic diseases are manifested.

Acute periodontal abscess on inspection is edematous and red with a smooth shiny surface and the area is dome like and relatively firm or pointed and soft (Figs 54.26 and 54.27). In most cases there is pus discharge from the gingival margin with gentle digital pressure. There is presence of periodontal pocket on probing. This is accompanied by symptoms like throbbing, radiating pain, exquisite



Fig. 54.24: Periodontitis—pus discharge visualized by using the ball of the index finger



Fig. 54.23: Healthy gingiva



Fig. 54.25: Deep periodontal pocket with inflammatory gingival enlargement



Fig. 54.26: Acute periodontal abscess (arrow)

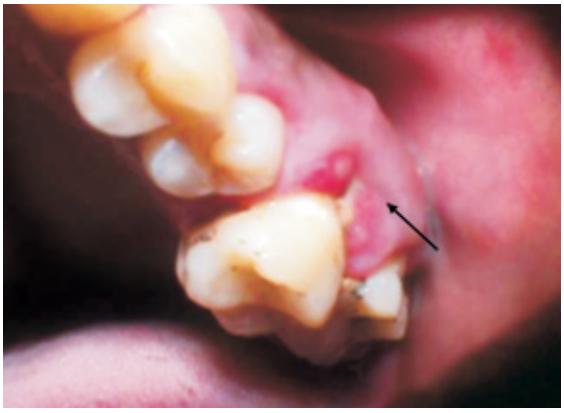


Fig. 54.27: Periodontal abscess (arrow)

tenderness of the gingiva to palpation, tooth mobility, lymphadenitis and less frequently systemic effects such as fever, leukocytosis and malaise.

Periapical abscess is present more towards the apex of the root but in children it can also appear on the lateral aspect. There is presence of a deep carious lesion or a nonvital tooth (the tooth is discolored—brownish, vitality test is negative).

Gingival abscess is found on the marginal gingiva and occurs in previously disease free areas. It is due to the impingement of foreign bodies resulting in an abscess.

Pericoronitis

On examination the pain is related to partially erupted tooth particularly the third molars. The tooth is covered by flaps of gingival tissue (operculum). The operculum will be acutely inflamed, red and edematous. Opposing tooth can dent or ulcerate the operculum. The pain may be spontaneous and is often exacerbated by closing the mouth. The pain may be aggravated by swallowing and there may be occasional fever and malaise.

BLEEDING FROM THE GUMS

Bleeding is assessed by running a periodontal probe along the soft tissue wall of the gingival crevice. It is given a score from 0 to 3. This is the gingival index by Loe and Silness. It is a method of assessing the severity and quantity of gingival inflammation in individual patients or among subjects in large population groups.

Score 0: Normal gingiva

Score 1: Mild inflammation—slight change in color and slight edema; no bleeding on probing.

Score 2: Moderate inflammation—redness, edema and glazing; bleeding on probing.

Score 3: Severe inflammation—marked redness and edema; ulceration; tendency for spontaneous bleeding.

The most common cause of chronic and recurrent bleeding is chronic inflammation as a result of plaque and calculus accumulation.

Acute episodes of bleeding occurs as a result of injury.

Spontaneous bleeding or bleeding on slight provocation occurs in acute necrotizing ulcerative gingivitis. Hemorrhagic disorders in which abnormal gingival bleeding is encountered include scurvy, platelet disorders (thrombocytopenia and thrombocytopathy), hypoprothrombinemia (vitamin K deficiency) and other coagulation defects (hemophilia, leukemia, Christmas disease), deficient platelet thromboplastic factor (PF3) resulting from uremia, multiple myeloma and post-rubella purpura.

Other rare causes of bleeding includes anticonvulsant drug medication, calcium channel blocking

drugs, immunosuppressants, antiplatelet drugs and thermal and chemical burns of the gums.

Changes in Color of the Gingiva

The normal coral pink color of the gingiva is red in inflammation with a bluish hue in chronic inflammation. The redness is limited to the marginal gingiva in acute necrotizing ulcerative gingivitis with punched out crater like depressions of the interdental papilla and covered with a pseudomembranous slough and demarcated from the normal mucosa by a linear erythema. Sometimes the lesions are denuded of the surface pseudomembrane, exposing the gingival margin which is red, shiny and hemorrhagic.

When there is diffuse, erythematous, shiny involvement of the gingiva and the adjacent oral mucosa the differential diagnosis may be erthythema multiforme, Stevens Johnson's syndrome, bullous lichen planus, desquamative gingivitis and recurrent aphthous stomatitis.

The gingiva may be pale in anemia and leukemia and yellow tinged in jaundice. Localized patches of dicoloration ranging from bluish black to brown is seen in Addison's disease and Peutz Jegher's syndrome. Albright's syndrome and von Recklinghausen's disease produce areas of oral melanin pigmentation. Blue gray pigmentation of the oral mucosa is seen in hemochromatosis. Pregnancy and diabetes can produce pigmentation in the oral mucosa. Polycythemia leads to deep red color of the gingiva. Heavy metals like bismuth, arsenic, mercury, lead and silver absorbed systemically from therapeutic use or household environments can discolor the gingiva. Typically metals produce a bluish or bluish black line in the gingiva that follows the contour of the margin.

Changes in Consistency of the Gingiva

Acute and chronic inflammations produce changes in the normal resilient consistency of the gingiva. The gingiva is edematous in acute inflammation. In chronic inflammation there can be fibrotic areas as well. Firm leathery consistency is found in gingival fibromatosis. The gingiva can even cover the teeth and interfere with the normal eruption patterns.

Changes in Texture

Smooth surface texture is found in atropic gingivitis as in desquamative gingivitis (Fig. 54.28). Hyperkeratosis results in a leathery texture, and drug induced gingival overgrowth produces a nodular surface.

GINGIVAL ENLARGEMENTS

Inflammatory enlargement of the gingiva occurs in acute and chronic gingivitis. The color is more reddish, smooth texture, soft in consistency with tendency to bleed (Fig. 54.29).

Drug induced gingival enlargement with anticonvulsants like phenytoin sodium, immuno suppressants and calcium channel blockers produces painless, bead like enlargement of the interdental papilla and the facial and lingual gingival margins that later coalesce. It may become



Fig. 54.28: Desquamative gingivitis



Fig. 54.29: Inflammatory gingival enlargement



Fig. 54.30: Drug induced gingival hyperplasia



Fig. 54.32: Mucocele of gums



Fig. 54.31: Idiopathic gingival enlargement

secondarily infected. The enlargement is fibrotic with a coarse texture. When secondarily infected there is bleeding and the surface is smooth and the consistency is soft and edematous (Fig. 54.30).

When the enlargement involves the interdental papilla and the marginal gingiva and it can cover the teeth, the enlarged gingiva is firm and leathery and characteristically with a minute pebbled surface. Massive enlargement of the gingiva which can cover the surfaces of the teeth and even interfere with tooth eruption is seen in idiopathic gingival enlargement (Fig. 54.31).

Pregnancy tumor is a discrete, mushroom like, flattened spherical mass that protrudes from the gingival margin or from the interproximal space attached by a sessile or a pedunculated base. It is dusky red or magenta has a smooth glistening surface that exhibits numerous deep pin point markings. This can occur in the gingival margin alone or it can be generalized tumor like masses. It usually regresses after child birth.

Gingival enlargement occurs in puberty and it mimics chronic gingival enlargement. It is bluish red, soft, friable and has a smooth shiny surface. Hemorrhage occurs spontaneously or on slight trauma. Gingiva that is red, friable, granular and bleeds easily may be a feature of plasma cell gingivitis.

Bluish red enlargement of the gingiva with a shiny surface moderately firm in consistency and a tendency towards friability and hemorrhage spontaneously or on slight provocation may be leukemic gingival enlargement.

Leukoplakia can also take the form of raised irregularly shaped keratinous masses. Exophytic, irregular outgrowth or ulcerative lesions on the gingiva may be squamous cell carcimona—investigation; biopsy.

Darkly pigmented flat or nodular lesion characterized by rapid growth and early metastasis is a feature of malignant melanoma. In addition to this gingival enlargement can also be a presenting feature of cysts, benign and malignant tumors and malignant metastasis from distant sites.

Cysts of the soft tissues of the mouth include developmental cyst like dermoid and epidermoid cysts, lymphoepithelial (branchial cyst), thyroglossal duct cyst, anterior median lingual cyst, mucoceles, ranula and parasitic cysts. These can be confirmed by biopsy (Fig. 54.32).

CHAPTER

55 Investigations in Dentistry

Angel Jacob

Diagnostic tests in dentistry, Radiograpy, CT scan, Investigative procedures in oral mucosal disease

DIAGNOSTIC TESTS IN DENTISTRY

In order to arrive at an accurate diagnosis and for the execution of a proper treatment plan, it is essential that investigations can be done to confirm the clinical findings. In addition to the physical examination, blood, urine, and tissue specimens are obtained from the patient and subjected to histological, biochemical, microbiological or immunological examination.

Investigations in dentistry can be divided into three phases:

- Routine dental tests
- Routine medical tests
- Additional tests.

Routine Dental Tests

- Vitality tests
- Thermal vitality tests
- Cold
- Heat
- Electrical vitality tests.
- *Thermal vitality tests:* A healthy tooth with a vital pulp can be stimulated within a temperature angle of 20 to 50°C without pain. Teeth with pulpitis may react with severe pain on temperature below the above range. Extremes of temperature are employed in the thermal vitality tests.
- *Cold:* A pledget of cotton wool, held with a tweezer is soaked in ethyl alcohol and allowed to evaporate. The icy pledget is then applied on to the tooth. Other methods include cold water and frozen carbon dioxide.
- *Heat:* Warm water, tip of a heated instrument, gutta percha stick softened in flame, heated impression compound can be applied on the tooth surface.
- *Electrical vitality tests:* More controlled, graded stimulus in comparison to thermal tests.

When the pain is positive (normal): The tooth responds in a similar level to stimulation as other healthy teeth. This suggests that the pulp is vital and not inflamed.

When the pain is exaggerated but brief: Here the tooth responds more severely than other healthy teeth and/or to a lower level of stimulation and the painful stimulus lasts for less than 15 seconds. It responds more to cold than hot stimulus. This occurs when the pulpitis is reversible when the cause is eliminated.

When the pain is exaggerated and prolonged: Here the teeth responds more severely and the painful response lasts for more than 15 seconds. Response to heat and electrical stimulation is greater than cold and cold stimuli may reduce pain. This is due to irreversible pulpitis.

When the response is negative the pulp is non-vital and necrotic.

Percussion Tests

Conducted by gently tapping a tooth with a tip of a dental mirror handle.

Two characteristics are noted: Tenderness to percussion and a dull percussion note. Both of these

denotes inflammation and accumulation of fluid. Greater tenderness to percussion in an apical direction suggests apical periodontitis. Greater tenderness to percussion in a lateral direction suggests acute periodontitis. Like vitality testing a number of teeth should be tested in addition to the suspected tooth and testing should begin on the healthy tooth.

Mobility of Teeth

Tooth mobility is assessed by use of two instrument handles one placed on the buccal and other on the lingual aspect of the tooth. Alternatively, a finger may be substituted for one of the instruments.

Increased mobility is caused by reduced bone support like periodontitis, neoplasms, cysts, abscess or inflammation of the periodontal ligament like apical periodontitis, periodontal disease, trauma or traumatic occlusion, crown or root fracture or fracture of the supporting bone.

Transillumination

It is useful in the diagnosis of interproximal caries of anterior and posterior teeth. Intraoral transillumination in a darkened room has been employed in the diagnosis of maxillary sinussitis.

Biting on a rubber, wood point, rubber dam material helps in the diagnosis of a cracked tooth.

Auscultation with a stethoscope placed over a temperomandibular joint may assist in the diagnosis of joint clicks or crepitus.

Diagnostic Local Anesthesia

Dental pain particularly due to pulpitis is difficult to localize. The patient may not even be aware from which jaw the pain arises. Elimination of pain by nerve blocks helps to localize the correct jaws. Infiltration can be used to localize the particular causative tooth.

Temperature of an accessible facial swelling can be gauged by placing the back of the operator's ungloved fingers on the swelling.

RADIOGRAPHY

Bite Wing Radiograph

This helps to assess the crowns of teeth, interproximal caries, restorations, alveolar bone height, over hanging margins of restorations and height of pulp chambers.

Intraoral periapical radiograph: This helps to assess the root and surrounding bone.

Orthopantomograph

This helps to have a general survey and shows the antrum and the temporomandibular joints and the radiation dose is considerably lower than a full mouth survey using periapical radiography.

Radiovisiography

Radiovisiography (RVG) is used particularly when there is need for repeated films. It is useful in reducing radiation exposure.

Sialography

Sialography involves injection of a radiopaque contrast media into the salivary duct followed by oblique lateral, posteroanterior or rotated posteroanterior radiographs. Silalography helps to assess patients with xerostomia, salivary swelling, ductal obstruction and salivary aplasia.

Arthroscopy

Arthroscopy involves injection of a radiopaque contrast media into the lower space of temporomandibular joint. The main indication is in suspected internal joint derangements.

Stereoscopic Radiography

This is used in detailed examination of fractures.

CT Scan

It is useful in the detection of oral cancers, fractures, maxillary sinusitis of dental origin. In order to distinguish maxillary sinusitis and sinusitis secondary to dental infection, a properly angled periapical radiographs along with panoramic view will give definite idea regarding any sinus lesions like mucosal hyperplasia, mucosal build up in the sinus floor or complete opacification. This can be confirmed by a corresponding CT scan. The resolution should be confirmed with a follow-up radiograph or a CT scan. The increased use of digital CT imaging is of great value in the diagnosis and follow-up of maxillary sinusitis of dental origin.

Soft Probes

These are endodontic silver points or gutta percha that may be inserted along sinuses and viewed

radiographically. In a similar way, needles can be inserted into tissue to localize a foreign body.

INVESTIGATIVE PROCEDURES IN ORAL MUCOSAL DISEASE

Procedures

Biopsy

If a vesiculobullous disorder is suspected, mucosal biopsies should be submitted for histopathological and direct immunofluorescence examinations.

Excisional biopsy: Biopsies can be excisional if the lesions are smaller than 1 cm in diameter and used when the clinician is fairly certain that the lesion is benign.

Incisional biopsy: This is applicable if the lesion is large and there is suspicion of malignancy. This is contraindicated in pigmented and vascular lesions.

Punch biopsy: This is used to punch out a representative portion of tissue. The resulting specimen is often damaged by the procedure and so biopsy by scalpel is preferred.

Needle/trephine/drill biopsy: This is employed to biopsy deep seated fibro osseous lesions.

Aspiration biopsy: Aspiration biopsy: It is applicable to cystic and fluctuant lesions.

Exfoliative cytology: Microscopic study of cells exfoliated or scraped off from the surface of the lesion.

Oral smears for cytology—sample cells are taken from the surface of the lesion. Oral brush biopsy is used to obtain cells from all three layers of the epithelium, the basal, intermediate and superficial layers. This is done in oral mucosal lesions.

Microbiology test: It is helpful in identification of the pathogenic microorganisms.

Polymerase chain reaction: For rapid and specific results DNA studies by polymerase chain reaction can be used.

Immunostaining and immunofluorescence: Direct immunofluorescence is used to detect immune deposits (antibodies and/or complement) in the tissues. Indirect immunofluorescence is used to detect immune deposits in the serum.

Fine needle aspiration cytology: Lymph node FNAC and FNAB can be done if malignancy is suspected and if it cannot be subjected to open biopsy.

Main Indications of Biopsy

Lesions that have neoplastic or premalignant potential. Lesions not responding to treatment or progressing despite treatment like leukoplakia and erythroplakia. Persistent lesions failing to respond to treatment like ulcers or radiolucent and radio-opaque bone lesions. Persistent lesions of uncertain etiology of soft or hard tissue. Persistent focal lesions involving the gingiva or periodontium and nonhealing extraction sites.

Biopsy can be done to confirm clinical diagnosis.

Hematological screening, hemoglobin, red cell and white cell indices: Essential to exclude systemic causes of oral diseases especially in case of ulcers, glossitis or angular stomatitis.

Serological analysis: This is done in suspected HIV infection, autoimmune and other immunological disease and connective tissue disorders.

Recent Advances

Biomarkers are used for assessing the risk for periodontal disease, dental caries and other mucous membrane disorders can be used. The samples can be obtained from saliva or gingival crevicular fluid.

Biomarkers in Periodontal Disease

A number of enzymes, tissue breakdown products, and inflammatory mediators are released from host cells and tissues during the development and progression of periodontal infections. Some of these substances have been suggested as possible markers for the detection of progressing periodontal lesions. These can be obtained from saliva and the gingival crevicular fluid.

Host-derived enzymes like matrix metallo-proteinases.

Host-derived inflammatory mediators like inflammatory mediators in gingival crevicular fluid including prostaglandin E2, interleukin-1β and interleukin-1, acute-phase proteins, and immuno-globulin types and subclasses, have been associated with disease severity and progression.

Tissue breakdown products like hydroxyproline, pyridinoline, collagen telopeptides, osteocalcin, and osteonectin.

This is especially important because recent studies have shown that periodontal disease is a risk factor for many systemic diseases like coronary artery disease, atherosclerosis, myocardial infarction, preterm low birth weight infants, pneumonia and poor glycemic control of diabetes.

Biochemical markers for dental caries such as nitric oxide and its metabolites, IgA and microbiological analysis for the presence of *Streptococcus mutans*, lactobacilli and actinomycetes species can be performed for assessing the risk and presence of dental caries.

Biochemical markers for oral mucus membrane diseases like lichen planus, specific antigens in stratum granulosum and stratum spinosum, tumor necrosis factor or oxidative stress markers can be assessed.

Cytogenetic aberrations can be used as markers for assessing the risk of development of oral cancer.

Recently, in addition to visual and tactile examination, bitewing radiographs, and fiberoptic transillumination, other technologies have been introduced to diagnose early stages of carious lesions. These include electrical conductance measurements, multiphoton imaging, ultrasound and quantitative fluorescence analysis.

Thermovision technique is an efficient tool for the diagnosis of physiological state and acute and chronic pathology of mucus membrane of the oral cavity. Both, physiological and pathological states are characterized by significant differences in temperature distribution.

SECTION

20

Statistics and Clinical Epidemiology, Research Methodology for the Beginner and Community Medicine

CHAPTER

56

Introduction to Statistics and Clinical Epidemiology–I

V Raman Kutty

Basic epidemiology for the clinician, Elements of statistics, Approaches to statistical inference, Testing of hypothesis, Interpretation of screening tests, Evidence based medicine

UNDERSTANDING RESEARCH—THE ROLE OF EPIDEMIOLOGY AND STATISTICS

Basic Epidemiology for the Clinician

A practicing physician should be able to critically read and selectively absorb the current medical literature. Most medical literature reports on occurrence of disease or disease related events. Such reports and studies incorporate epidemiological thinking and reasoning, since epidemiology is the science which studies the occurrence of disease in populations. It may be extended to cover all phenomena related to disease, such as:

a. Frequency of occurrence of disease
b. Frequency of occurrence of consequences of disease (be they complications or cure)
c. Frequency of association of disease with other factors (frequency of co-occurrence).

Frequencies can be formally expressed in many ways:

1. As incidence density
2. As incidence proportion (cumulative incidence) and
3. As prevalence proportion.

Disease event frequencies are expressed as counts (of events—*the numerator*) in relation to a *denominator*. In all three types of disease frequency measures, the numerator is the same—the disease count. The denominator, however, is different for the three different measures.

Incidence Density (Person-Time Incidence Rate)

This is frequency of disease events expressed in relation to the subjects as well as time; such as 'an incidence rate of stroke of 5 per ten thousand per year'. This is the same as saying that after following ten thousand persons without stroke for a period of one year, 5 were found to develop it by the end of the period. This is also expressed as *5 per ten thousand person years*—this statement suggests that the disease goes on occurring at this rate. An incidence rate may vary from 0 to infinity. Incidence rate has dimension, i.e. the magnitude of the rate depends upon the unit used to measure time—the same rate expressed in person years will be different from that expressed in person months. In the previous example, the rate of 5 per ten thousand person years will be equivalent to 0.42 per ten thousand person months.

Incidence Proportion

Incidence proportion, sometimes called cumulative incidence is the proportion of initial subjects who develop the disease within a fixed period of time. This can be expressed as a fraction of the total—an incidence proportion of 1% (0.01) in one year means that one out of hundred subjects becomes diseased in a period of one year. It is possible that none fall ill during any period, or all may fall ill. Hence, like all proportions, cumulative incidence can vary from

0-1 (0%–100%). In the previous example of stroke, the cumulative incidence will be 0.0005 or 0.05% in one year, in whatever way it is measured.

Prevalence Proportion

Prevalence proportion indicates the proportion of people who are sick at one point of time, compared to the whole population. This can also vary from none to all, or in other words, from 0 to 1. In estimating prevalence, we do not take the time element into consideration—it is like a still photograph of a sportsman which freezes the action. From the photograph, we are not able to gauge the strength or speed of the action. A disease can spread so fast as to kill almost every body in a community, and thus, leave a low prevalence. Diseases which neither get cured nor lead to fatalities can have a high prevalence. Low back pain and chronic headache would be examples. Thus, prevalence is dependant on the rate of occurrence as well as the duration.

Risk and Its Assessment

Much of medical research is concerned with 'risk' and its assessment. Risk simply means the chance—or the probability—of an event happening to a person. In medical research, this event can be occurrence of disease, occurrence of complications, death, recovery or hospitalization. Risk is usually estimated by the incidence proportion—the incidence proportion of disease in a group of people is a measure of the group's average risk for the disease for the relevant time interval. Note that risk is always expressed with reference to a group, and a period of time. Thus, when we talk about the annual risk of tuberculosis among smokers, the lifetime risk of lung cancer in men, or the five year risk of breast cancer in women over the age of thirty, it would be equivalent to what the incidence proportion of the disease would be in a group with similar characteristics observed for the relevant period of time.

Often we are interested in how much higher the risk of disease is in a group with a certain characteristic, when compared to one without the characteristic. Thus, when we ask the question, 'Is the risk of breast cancer higher in obese as compared to nonobese women?' we are making a comparison of risk in two groups, i.e. obese and nonobese women. If the risks—or incidence proportions—in both groups are the same, we would expect the ratio of risks to be unity (or 1). Any ratio where the group with the characteristic— often called the 'exposed' group—has a higher risk in comparison to the group without the characteristic—the 'unexposed' group—will be higher than one. This ratio is called the 'relative risk', or 'risk ratio', and is often shortened to RR. This ratio can be lower than one if the 'exposed' group has a lower risk, as when the exposure is protective, like a vaccine.

Among the measures of disease frequency, incidence measures give an indication of the force of attack of a disease—how fast it is spreading in the population. Hence, studies reporting incidence rates are important in prioritizing intervention programs. Prevalence measures give us an idea about the burden of disease at any moment of time, and are important in planning services. Relative risk measures associated with an exposure indicate how important the exposure could be as a causative factor in the disease. This is especially important in chronic diseases which have many potential risk factors.

Odds Ratio

'Odds' is a concept related to probability, and therefore to risk. If 'p' is the probability of an event occurring, then it follows that the probability of the event not occurring must be 1-p. The ratio p/ (1-p) is called the 'odds' of the event. The probability of a fair coin turning up heads is ½, so the odds of the event is (0.5/0.5) = 1.

We have learnt earlier that the relative risk, or the ratio of risks, can be expressed as:

$$\frac{\text{Probability of the event in exposed}}{\text{Probability of the event in unexposed}}$$

Similarly, the odds ratio can be calculated as:

$$\frac{\text{Prob (event) in exposed/1-Prob (event) in exposed}}{\text{Prob (event) in unexposed/1-Prob (event) in unexposed}}$$

Odds ratios are often reported in medical literature. This is mainly because the odds ratio is practically the same as the risk ratio *when the event under scrutiny has a small probability,* as most

medical events have. So whenever the literature discusses odds ratios, we can take them to be the equivalent of risk ratios. Thus, when an odds ratio, shortened as OR, for an event is higher than 1 in a group with a certain characteristic, it means that the group has a higher risk of getting the event when compared to a group without the characteristic.

ELEMENTS OF STATISTICS

Measures of Expectation or Averages

Most investigations measure or estimate some quantity or other. This may be subjects' height or weight, or it may be some biochemical value such as fasting blood sugar, serum low density lipoprotein cholesterol (LDLC), or uric acid. Often the measurement made is of an event such as the incidence rate of cataract in people over the age of fifty years. The investigator wants to know about this measure in a large group of people. This group is generally called the 'population' or the 'universe'. The population or the universe consists of all the individuals or units about whom we want to make an inference. In a study about malnutrition in women in a particular village, the universe or the population for the study consists of all the women in the village. In a study about the efficacy of streptokinase in coronary heart disease among patients admitted to a particular hospital, the universe consists of all such patients. But in most cases, the investigator is not able to study all the individuals in the universe. He or she has to select a 'sample' or a small group from among the universe or population. The study is limited to this sample, but the inferences are made about the whole population.

The process of selecting a sample is called *sampling*. In most scientific studies, some form of probability sampling is employed. Probability sampling is a method where we can compute the exact probability of each individual in the population being selected in the sample. The most common technique of probability sampling is simple random sampling. This means that the sample is drawn using some method which generates random numbers, such as using a random number table or using a computer program. *This does not mean that the sample is drawn haphazardly.* Suppose from a population of one hundred, a ten percent sample is drawn randomly. Here each element in the population has a 10% chance of being selected in the sample, or, in other words, the probability of selection of each of the elements of the universe in the sample is 0.1. Other methods of probability sampling are systematic sampling, stratified random sampling, and cluster sampling. The advantage of probability sampling is that it helps us to make a reliable and valid inference about the population from the sample.

Measurements can be made with varying degrees of precision. The characteristics which we measure are sometimes called '*variables*' since they vary in value from one subject to the next. In some instances, the attribute or the characteristic which we want to measure can only be put in categories. Patients can be either male or female. Subjects may have a disease or do not have it. Such types of variables are called 'categorical'. Often we can rank subjects on the basis of the presence of the attribute—pregnant women can be in the I, II, or III trimester of pregnancy. Complications from a disease can be ranked as life threatening, serious, and minor. Such variables, where there is an implicit ranking, are called 'ordinal'. There are some attributes where the measurement can be made with any degree of accuracy. Height can be measured in centimeters, millimeters, or in fraction of these. Glucose level in blood can be measured in milligrams or even in finer units. These are called 'continuous' variables.

When the investigator makes measurements or estimations on a number of subjects in a group or sample, he or she often has to summarize the observations for communication, because it is cumbersome to represent each and every measurement in a concise article or paper. Summarization of categorical variables is easy because they can be represented as a table of categories with counts of subjects in each category, with each attribute properly labeled. Ordinal variables can also be so represented. In the case of continuous variables, we often employ some summary value which represents the group which is measured. This summary value is dependent on the frequencies of occurrence of various values in the group. Since the value should represent the group, this is often some sort of an average value which is the 'expectation' for that attribute in that group. Often the most commonly occurring value is used—this is the '*mode*'.

Sometimes the central value of the one which divides the group into two equal halves if they are ranked from the lowest to highest—is used. This is called the *'median'*. The most commonly used measure of summarization is the arithmetical average—adding up all the values and dividing by the total number of subjects. The measure we employ in this case is called the *'mean'*.

The mean, mode or median gives us one value which represents the group. But this alone does not summarize the measurements in the group. Groups may be very different with respect to the variation within them. An estimate of the variability within the group is given by a measure called *'variance'*. We get the variance by taking the difference of each individual value from the mean, squaring it, adding the squared values together, and taking their average—the average of the squared differences. Often, a measure called *'standard deviation'* is employed instead of the variance. This is simply the square root of the variance.

Why do we want measures such as the mean and the standard deviation?

One major reason is to describe the group with respect to the characteristic (descriptive statistics). Men and women, as well as people of different nationalities, vary with respect to their height; this can be represented as the mean heights and standard deviations in each group. This makes the comparison of groups easy. Another important reason arises when we take a small sample from a large population in order to study the characteristics of the population —since we are not able to study every individual in the population, we have to make inferences about the population from the sample (statistical inference). The mean and standard deviation help us to do that. Depending upon certain assumptions about the distribution of values in the universe or population, (which we will not go into here), and using the mean and the standard deviation of the sample, the process of statistical inference helps us to make some statements about the population characteristics.

APPROACHES TO STATISTICAL INFERENCE

Confidence Intervals

Very often in the literature, we come across an estimate, with a 95% or 90% confidence interval or confidence limits given alongside. The mean height of 1000 men in a factory, estimated from a sample of 100, can be 165 centimeters (95% confidence interval, 160–170). In another example, the estimated prevalence of coronary heart disease in a district, computed from a random sample of 1500 adults, is 35/1000 (90% confidence limits 32, 38). The first statement implies that we can say with 95% confidence that the true mean height of the 1000 men in the factory, the parameter that we set out to estimate, lies within the interval 160–170. There is a 5% chance that the true mean height is not within these numbers. Similarly we are 90% sure that the true mean prevalence of coronary disease in the district is within 32 to 38 per thousand. Confidence estimates may be generated around incidence rates, prevalence values, odds ratios or any estimate of a population parameter from a randomly drawn sample.

Testing of Hypothesis

Confidence intervals constitute one type of statistical statements. There is a tendency for more and more journals to insist on reporting of confidence limits in papers submitted to them. There is another format for statistical inference which used to be much more widely used, and is still quite popular. This is called 'hypothesis testing'. A hypothesis is a statement about a characteristic or relationship in the population of interest which the researcher wants to explore.

Research hypotheses are stated as 'null hypotheses'. The researcher puts it in a negative way, though it may not actually be so stated in the article. A physician wants to see if routine use of a new anti-inflammatory agent X, reduces pain in the joints. He has a research question, "Does the use of drug X in a dose of 500 milligrams three times daily for five days relieve joint pain in 50% of sufferers of severe rheumatoid arthritis?" This question is reformulated by the researcher as a null hypothesis: "Use of drug X in a dose of 500 milligrams 3 times daily for 5 days, does *not* reduce joint pain in 50% of sufferers of severe rheumatoid arthritis". Note that research questions, as well as null hypotheses, are precisely stated and very specific as to the population (sufferers of severe rheumatoid arthritis), intervention (drug X in a dose of 500 mg 3 times daily for 5 days), and the estimate of the effect (50% reduction in pain).

Testing a null hypothesis has often been compared to the working of the judiciary. A man charged for a crime is brought before a court. He is presumed innocent—till the prosecution can prove that he is guilty. If they fail in this, we say that there is no evidence to prove his guilt. Similarly a null hypothesis is presumed to be true till the researcher can produce information which leads us to believe that we should reject it. If the researcher fails in this, the null hypothesis continues to be held and we say that there is no evidence to reject the null hypothesis.

Research	Judiciary
1. Null hypothesis presumed true	Accused presumed innocent
2. Information collected	Evidence produced
3a. Information insufficient Null hypothesis not rejected	Evidence insufficient Accused not convicted
3b. Information sufficient Null hypothesis rejected	Evidence sufficient Accused convicted

Why is the prisoner presumed innocent/null hypothesis presumed to be true?

There are two types of mistakes the judge can make:

1. Concluding that the prisoner is guilty when in fact he is innocent
2. Concluding that the prisoner is innocent when he is in fact, guilty.

"Even if a thousand guilty persons go free, not even a single innocent person should be punished".

Type 1 mistake is the more serious one. We want to avoid it at all costs. Similarly, in research, rejecting a true null hypothesis is considered a more serious error than not rejecting a false null hypothesis.

Conclusion from Trial

	Actual situation	
	Guilty	Not guilty
Guilty	Punishment to the accused—correct decision	Innocent person convicted more serious error
Not guilty	Guilty person let free—less serious error	Accused person set free—correct decision

Conclusion from Research

	Actual situation	
	H^o not true (true difference between test and control)	H^o true (no true difference between test and control)
H^o rejected:	Conclusion: There is a difference	Finding a difference when there is none—more serious (Type I) error—alpha error
H^o not rejected	Finding no difference where it exists—less serious *(Type II) error-beta error*	Conclusion: There is no difference

Since we consider alpha error or type I error to be the more serious error, we want to keep it down to a low level. By convention, this level is fixed at 1/20 (0.05) or below:

Process of statistical inference consists of the following steps:

1. Formulate the research question
2. Set up the null hypothesis
3. Decide the alpha error rate
4. Look at the data
5. Use appropriate statistical tests
6. Conclude whether H^o is to be rejected or not.

Statistical "significance" though we have fixed an alpha error rate before we embark on statistical testing, the procedure gives us a 'p' value or *probability of having committed an alpha error.* This tells us whether the data support the null hypothesis or not. $P<0.05$ (or any other predetermined level) means:

1. We reject H^o, but there is a 0.05 chance that we are making a mistake (alpha error).
2. If the null hypothesis (that there is no difference) were true, the probability of observing these data would be as low as this—hence the null hypothesis is unlikely to be true.

The term "statistical significance" is to be treated *strictly as a technical term*, meaning that the data showed a "p" value below the predetermined alpha error rate. This is to be distinguished from actual or clinical significance, which is a measure of the importance of a finding in practice or real life. In fact, it is advisable to avoid the term "significance" except in the technical, statistical sense. Often statistically significant results are of the least

importance in life (except if you are looking for a publication!), and sometimes findings of great clinical portent may turn out to be statistically not significant (we should not say 'statistically insignificant', by the way) because there were not enough number of subjects in the study.

Beta error rate is the chance of not rejecting a H^o which is actually not true (which means you are unable to detect a true difference using this test, which in some way relates to the capability of the test procedure). If this chance is very high, that means the capability of the test is very low. Hence (1-Beta) is called the *Power of the Test.*

INTERPRETATION OF SCREENING TESTS

In the course of clinical practice, we are called upon to do and interpret a number of laboratory and other tests. Sometimes tests are used to 'screen' for a rare disease, i.e. to find out how many of the screened people are highly likely to have the disease. This is especially true of cancer, cardiovascular disease such as coronary disease, hypertension, HIV status, and many other chronic conditions. Screening helps clinicians to identify early cases and institute treatment, thereby avoiding serious consequences later. Usually, a screening test is a less costly test which indicates which subjects are likely to have the disease, so that they can be investigated in full.

However, when we apply a screening test, or any laboratory test to a person, there is the likelihood of one of two types of mistakes happening:

a. A person without the disease may be labeled by the test as having disease—this is called 'false positive'
b. A person with the disease may be missed by the test—this is called 'false negative'.

This is demonstrated by the following diagram:

Test status (inference from the test)	*Disease status (true state of affairs)*		
	Having disease	*Not having* disease	
Test positive	a = true positive	b = false positive (test positive without having disease)	a + b = all who tested positive
Test negative	c = false negative, (test negative but having disease)	d = true negative	c + d = all who tested negative
	a + c = all with disease	b + d= all without disease	a + b + c + d = all who were tested

Contd...

Prevalence of disease = a + c/(a + b + c + d)
'*sensitivity*' of a test refers to the ability of the test to identify true disease—out of 100 persons with disease, how many would be correctly classified by the test as having disease? It can be seen that it is estimated by (a/a+c). Similarly, *specificity* is the ability of the test to identify truly those without disease—out of 100 persons without disease, how many would be correctly classified as not having disease? This is estimated by (d/b+d). A test has two additional characteristics—the *positive predictive value and negative predictive value*. Positive predictive value (a/a+b) indicates what proportion of those testing positive will be truly positive; negative predictive value (d/c+d), in a similar vein, indicates the proportion of truly negative subjects out of those testing negative. *Sensitivity and specificity are attributes of the test; positive and negative predictive values depend also on the prevalence of disease*. In other words, positive predictive value of a test is a characteristic of the test as applied to a population; it changes if the same test is applied to another population. For example, if we apply a test with 99% sensitivity and 99% specificity to a population where the prevalence of disease is 1per thousand (0.1%), then the positive predictive value is only around 9%; or in other words, around 91 people out of every 100 who tested positive will be false positives. When the same test is applied to a population where the prevalence is as high as 10%, the positive predictive value shoots up to 91% (This can be checked by putting in some hypothetical numbers in the table).

Likelihood Ratios

Before we do a laboratory or screening test on a patient, we have an idea of the probability of disease in the person, which is formed from history taking and our previous knowledge about the occurrence of disease in similar patients. For example, when a forty-five year old male comes to the casualty with

complaint of chest pain, the index of suspicion for myocardial infarction will be high. When we do a laboratory test, this is to confirm or reject our provisional diagnosis. This can be formally captured using epidemiological principles. Our notion about the chance of disease in the person before doing the test can be represented by the 'prior odds of disease', which is (Probability of having disease/1-probability of having disease) in the person. The probability of disease in any person can, for convenience, be equated to the prevalence of the condition in the population from which he comes. Thus in India, where roughly around 10% of adults may be expected to be diabetics, the 'prior odds of diabetes' in a random adult patient will be = (0.1/0.9) = 0.11. When we do a screening or lab test on a patient, we can apply a value called the 'likelihood ratio of a positive test' to these prior odds to get what is known as the 'posterior odds of disease'. The likelihood ratio of a positive test is given by the formula, (sensitivity/1- specificity). Thus, if an Indian community is screened for diabetes with a test (finger prick test) with a sensitivity of 95% and specificity of 80%, and a subject turns out positive, then the posterior odds of diabetes = prior odds × likelihood ratio = 0.11 × (0.95/0.20) = 0.52. From this, we can calculate the posterior probability as (posterior probability = [posterior odds/1+ posterior odds]) = 0.34, or 34%. Thus before testing, we thought the individual had a 10% chance of having the disease; if the test turns positive, we revise our estimate of his chance of having diabetes as more than three times our original estimate. The same thing applies if the test turns negative also; but in this case, we use the 'likelihood ratio for a negative test' as a multiplier. This ratio is given by the formula (1-sensitivity)/specificity. In this particular case, if the test turns out negative, multiplying the prior odds of having diabetes, 0.11, by the likelihood ratio of a negative test, ((1–0.95)/0.80), we get 0.062 as the posterior odds of not having diabetes, which translates into a probability of less than 1%. In the beginning, our estimate of the chance of the patient having the disease was around one in ten; after we get the test as negative, we revise our estimate to less than one in a hundred. The sensitivity and specificity of a test as well as the prior probability of disease (prior odds) play a large part in determining the interpretation of both positive and negative tests.

EVIDENCE BASED MEDICINE

Medicine is an ever changing science. What was accepted practice yesterday is often questioned today, and what is the gospel truth today, would be subject to scrutiny tomorrow. Hence, the practitioner is often at a loss to understand, evaluate and digest the trends at the pace at which they occur. Ideally, a doctor should undertake only such diagnostic and therapeutic procedures as have been shown to be efficacious. This is because administering an unproven drug or intervention would put the patient to unnecessary risk. However, many drugs are introduced in the market with claims to high levels of efficacy. Doctors sometimes find it difficult to evaluate the weight of evidence in favor, or against such claims. In modern times, the volume of information that is available to the practicing physician has increased exponentially, so much so that one finds it difficult to deal with it. It then becomes imperative to have yardsticks for deciding which articles should be trusted more with respect to their findings. In this quest, knowledge of research design and epidemiology plays an important part.

The concept of *'evidence based medicine'* has gained popularity in recent years. It is an approach that tries to instill in clinicians a healthy skepticism about clinical practice, and arm them with tools to examine the evidence in favor of new, as well as old, therapeutic and diagnostic interventions.

A doctor learns the elements of her practice from her teachers, textbooks, and from her seniors and colleagues in the wards. As she graduates and starts to practice, she depends on her own experience. She adds to this what she learns from continuing education programs, and articles in medical journals. It is important to develop a critical faculty for ranking these inputs in the order of their credibility.

Even though what we learn as students remain important, it is crucial to subject them to scrutiny very often. A mode of examination, a diagnostic test, a therapeutic intervention may go out of vogue, because newer methods have been discovered. Should we continue to hold on to the old method, or should we abandon those and whole heartedly accept what is new? As extreme cases, we all know of people who never give up the ways they learnt as students, and continue to practice medicine exactly

the same way for fifty years; and those who jump on to any new bandwagon without critically examining whether it benefits the patient. Both are bad role models. How shall we sift the evidence?

Most new therapeutic and diagnostic approaches and drugs claim to be supported by 'scientific' studies. We should examine how scientific are the studies that support these claims. *Anything which has not been published in a medical journal does not merit a second look at all.* Even among published articles, make sure that these have come out in peer reviewed and indexed journals. How does one know if a journal is peer reviewed and indexed? Fortunately, it has become rather easy, since most peer-reviewed and indexed journals are abstracted by services such as Medline and Embase. So any journal which does not find its place in Medline (the online medical literature data base available free of cost on the internet, *courtesy* the National Library of Medicine, USA) should be viewed with skepticism.

Unfortunately not all articles published in the medical literature are fault free. The following check list will help one to decide on the credibility of reported results:

1. Does the article report a study conducted specifically to answer a question related to the intervention of interest, or is it a coincidental finding? Important results should always be confirmed by studies specifically designed for the purpose.
2. What is the design of the study? Is it descriptive or analytical? Descriptive articles, such as case studies or cross sectional surveys of populations, will report on various attributes, some of which may be of interest to us. However, we should not take information from such studies too seriously, as they may be chance findings. *Analytical studies* should be given more weight than descriptive studies. In analytical studies, two groups will be compared to arrive at an inference relating to a particular intervention, exposure or procedure of interest. This gives us an insight as to whether the intervention is efficacious in bringing about the desired outcome. This may relate to a vaccine preventing a disease, or a drug attaining a cure, or a pain killer bringing relief from pain. The greatest weight of evidence is given to *experimental studies,* where the investigator manipulates the conditions so that one group receives the intervention of interest and the other doesn't, and the outcomes are compared.
3. What is the size of the effect reported? Statistical significance alone should not be taken as the criterion to judge any finding. Sometimes a tiny effect can attain statistical significance, but it may not be important clinically. Size of the effect can be the proportion of people cured, the degree of pain relief, or any measurable outcome.
4. Who were the subjects in the study? Was there enough numbers, or was it a small study involving only a few subjects? Did the subjects include men, women and children? Are the subjects comparable in their ethnicity, habits and social and economic situation to the patients you want to treat, or should they be treated as a special group?
5. Is it a one time finding or has this been reported from elsewhere? A finding reported from several centers naturally merits more attention than isolated finding.
6. Finally, one also goes by such norms as the reputation of the journal which has printed the article, and the department which has conducted the study. Though one may argue that theses are very subjective criteria, commonsense dictates that these are perhaps the easiest criteria to judge by. General interest journals such as Lancet, New England Journal of Medicine, British Medical Journal and the journal of the American Medical Association generally command greater credibility because their peer review process is much more stringent.

Most articles discuss association between an outcome, such as disease event or complication, and an attribute which is thought to be causative for the outcome. This attribute is technically called an 'exposure'. Study designs facilitate comparison among two or more groups. Of all such study designs, the *randomized controlled trial* (RCT) is thought to be superior since it deals with most methodological problems by random allocation of treatment groups, i.e. who gets exposed to the

intervention is decided randomly. This controls for the effect of other variables in influencing the interpretation, by balancing the distribution of these attributes in the two groups equally. The RCT further reduces error by masking (earlier term= 'blinding') the subjects as well as the investigator, so that comparisons are not influenced by personal beliefs. Thus, the RCT becomes the 'gold standard' for the ideal study. However, it is not practical to do RCTs for every research question, because most of these involve harmful exposures, and it is unethical to expose human subjects to such exposures. So we have to resort to 'observational designs', where either an unexposed group is compared to one or more exposed groups with respect to the outcomes (cohort design), or a group with outcome is compared to group without outcome with respect to levels of exposure (case-control design).

When we look for evidence of association between an outcome and an exposure (is physical exercise associated with protection from heart disease?), we may find many articles which may give inconsistent, or even conflicting answers. There is a hierarchy of evidence which helps us to decide how much importance we should give to each of these studies. Based on design considerations, we give the place of honour to RCTs—so if we can find a study where subjects have been randomized into two groups, one of whom has been intensively pursued to take up physical exercise and have done so, and compared heart disease among these two groups, this study will get the highest consideration. Other observational studies—cohort and case control— may get less importance. There may also be several RCTs reporting on the same association, with varying results—in this case, we have a way of combining information from all the studies to come up with one final answer. This statistical technique is called 'meta-analysis'; it is given the highest position in the 'evidence pyramid'. A meta-analysis usually goes through the following steps:

1. Set down the criteria for accepting a reported study as part of the meta-analysis. Here, the journal of publication, the methodology, the techniques of measurement, and the subjects of study may all be criteria for acceptability.
2. Search the literature for all studies fulfilling the criteria. This is usually done by computer, augmented by other methods.
3. Use statistical norms to give weight to findings from each study. These may be sample size (number of subjects studied), the rigour of exclusion and inclusion of subjects, comparability of techniques used for measurement, and effect size reported.
4. Combine results from all the studies statistically, so that the reviewer can report one main conclusion which incorporates evidence from all the studies.

Though the technique appears neat and appealing it has its own pit falls. For one, the search for reported studies may not yield comprehensive results, due to many reasons. Many a time, yield of a computer search depends on the search engine, the terms used and the skill of the person doing the search. Moreover, 'publication bias' may bedevil many searches. Most medical journals favor papers reporting positive results, i.e. those reporting that any new drug or procedure is efficacious, and they tend not to publish articles saying that these are not efficacious. Hence, a search of the published literature tends to yield many more papers reporting positive results than negative results.

Though we want the meta-analysis to be very objective, we can hardly avoid an element of subjectivity. This is because the analyst sets the criteria for selection of studies into the analysis, and these can often be very subjective. One great advantage of meta-analysis, however, is that it is able often to report an effect size which combines those from smaller studies, and this would be equivalent to doing one study with subjects from all the studies participating in it.

The Cochrane collaboration is a foundation setup exclusively to promote evidence based medicine. It is based in the UK, with sister foundations in many other countries. It was founded by Archie Cochrane, who supported the cause of randomized control trials to answer questions of therapeutic efficacy. They have compiled a database of all available RCTs to answer various therapeutic questions.

CHAPTER

57 Research Methodology for the Beginner

V Raman Kutty

Basic Concepts, What is research?, Research methods for physicians

BASIC CONCEPTS

Doing Your Own Research

Apart from understanding research that other people have done, there may be occasions when a doctor has to undertake research on her own. Very often, this is a requirement for masters' and doctoral degrees like MD or DM. National agencies such as the Indian Council of Medical Research (ICMR) also encourage medical students to be initiated into research. Occasionally a medical student is so fascinated by research that she decides to make it her career. Research may be undertaken with the support of an external funding agency, or from funds available within the hospital. It usually addresses some important questions within the hospital or community setting. It is important to know that research, especially in modern times, has a definite format and people engaging with it are expected to know and follow this format.

WHAT IS RESEARCH?

Research, though it sounds like a very esoteric activity undertaken by people with an abstract bend of mind, is in fact a very practical undertaking. It means nothing other than planned activity, usually leading to generation of information, which is specifically focused on answering a definite question. This is what we call the research question. The research question may come from reading of the literature, or from knowing some general facts about the population. It may be suggested by a colleague's conversation, or come 'out of the blue'.

Preparing for Your Research—What is Your Research Question?

The research question has certain characteristics—any question can't be a research question. It has to be an 'empirical' question, i.e. a question concerning observable or measurable elements. It also has to be stated in specific terms—if you want to know whether drug X is effective in rheumatoid arthritis, you have to specify what is the dosage of the drug, how long is the treatment expected to take place, in what group of people do you want to test the effect, and what is the outcome you are looking for. In other words, the research question has to talk about what (drug X), in whom (in women above the age of 50), how (oral pills), how much (dosage) and how long (duration of treatment), leading to what effect (relief from pain and lack of mobility as assessed clinically). The research question also has to be relevant—the problem has to be important in the population among whom you are working.

Preparing for Your Research—Reading the Literature

Very often, research questions occur to you on reading what other researchers have written. Reading the medical literature on the subject and knowing what is already known about it is important if you want to justify your own research. Sometimes you pick up a gap in the knowledge, and there is a need for research to fill up this gap. Often something that

has been demonstrated in some other population may need to be done in the local population for confirmation. Thus, reading the medical literature enables you to build up the background for your research and answer the question 'why is this research important?'

Medical literature is available in many forms. Most commonly, there are textbooks and journals. Journals are now a days divided into categories depending on their importance. Each scientific journal carries an 'impact factor'—a number which indicates the impact that any article in that journal will have among the medical readers. This reflects the credibility of the journal and is calculated taking into account many attributes such as the nature of the journal, the number of articles submitted to it, the review process, the areas of coverage and many other factors. The higher the impact factor, the greater the weight to be attached to any article published in the journal. Among medical journals, there are journals for the general medical reader, such as the Lancet and the New England Journal of Medicine which publish articles that are of interest to most medical readers. They generally have a higher impact compared to the specialty journals, which cater to a narrower breed of readers within each specialty.

Currently many journals are accessible on the worldwide web; however, many of them are freely available only to those who are subscribers. Some institutional libraries provide access to members of the institution to journal websites. However, abstracts (short summaries) of all articles published in journals are collected and published by indexing databases such as the Index Medicus, whose electronic, online version is called 'Medline'. Medline is made available to the public through Pubmed, a service of the National Library of Medicine in the US. If we search Pubmed, we will know what articles have been published in any indexed and peer reviewed journal in the subject in recent years. We can collect the abstracts which are of interest to us, and read them to know what research by other people have come up with. Index Medicus is not the only medical indexing database; there are many, some of which specialize in certain types of journals, including Excerpta Medica. Most of these, with the exception of Pubmed, however, do not come free of charge.

Apart from journals another important source of information about current state of knowledge in any field is the textbook. Textbooks contain authentic information, though they could be outdated, compared to journals. Some textbooks are also available through the worldwide web.

Dissertations and unpublished student work is another source of information on any topic, but they are more difficult to access because they are not listed systematically and available to everyone.

Preparing for Your Research—Writing up a Proposal

Having decided your research question and scanned the literature, you need to prepare a research proposal. This is needed if you want to apply to any external funding agency for support, as well as for most internal review committees. The research proposal or 'protocol' as it is sometimes called—usually has several parts. It is easily remembered by thinking '*why-what-how-in what time-at what cost*'.

Introduction

This covers the background for your study and justifies the need for it, based on current medical literature on the subject. In other words, it covers 'why' you want to do an 'what' you want to do.

Objectives

This section sets out the research question, and the specific objectives coming out of it, in measurable terms; 'what' you are trying to achieve.

Methods

This section covers 'how' you are going to do your research. It should have information on the number of subjects, details of the design of the study, how the information will be collected (through questionnaire, laboratory tests, other methods), and how you would later analyze your data.

Time Frame and Budget

Each proposal should be accompanied by a plan detailing the expected time for each of the activities under it and the total time for the project to be completed. The budget should include all the expected costs, including salaries, consumables,

travel costs, equipment costs, including costs for data analysis and writing up of the report.

Apart from the above, each proposal should also mention the ethical considerations of the particular research. There is an increasing awareness of the need to promote ethical research and to protect the rights of the subjects at all times. All proposals usually go before an institutional ethical committee or review board (IRB); it scrutinizes the proposal to see whether there is any potential harm to the subjects and whether they have been protected from it, what are the benefits accruing to them from the research, and whether their confidentiality would be maintained. It is the onus of the researcher to convince the review board on all these points.

RESEARCH METHODS FOR PHYSICIANS

Research in medicine and health usually employs one of the three broad general approaches—the clinical, laboratory, and field research. The general principles of research design, defining the universe of the research (the group of people your research findings would apply to), picking the sample, analysis and communication of the results would be broadly similar; the setting for the research, however, would vary in the three different types of approaches. Clinical research is done on patients or potential patients in a hospital setting. Field research involves going to the community to identify your subjects; very often the subjects may also be healthy individuals rather than patients. Laboratory research is done with either material collected from patients (such as blood or tissue- *in vitro* studies), or involves experiments done on animals (*in vivo* studies). Both clinical research and field research can be experimental—when an intervention is introduced in one group of subjects deliberately by the researcher and compared with another group which does not receive the intervention, or observational—when the researcher only collects information and follows up both groups to compare them. It can be descriptive when the objective of the research is only to describe a phenomenon in detail—as in case studies or surveys—or analytical when we try to find associations between outcomes and 'exposures'. An exposure can be any attribute such as a behavior like smoking or drinking, an ethnic identity or nationality, gender, age group, environmental exposures, or any characteristic which the researcher thinks might cause or prevent the outcome under study. Exposures are also called risk factors.

Before starting the research and as you develop the proposal, consult a statistician or epidemiologist for advice on issues such as design, sample size, and use of computer programs. Going to them after collection of data may not be of much use.

Data Analysis and Report Writing

Information which helps you to arrive at an answer to your research question is called *data*. This is collected through questionnaires, or from laboratory investigation results, or observations. Usually this is collected in a structured format, with all important details collected from each individual subject in the study using a 'proforma' or protocol. This protocol should be discussed with your co-workers and submitted along with the research proposal; after approval by the funding agency and review board, it is tested (pilot testing) on a small sample of subjects before finalizing. This helps to bring out any obvious mistakes or omissions. Data collected in protocols, from all subjects, needs to be entered into the computer before analysis.

Many computer programs help in entering, storing, correcting and analyzing data. It is very helpful to pick the program even as you start the research; in this way, data can be entered as it is collected. A simple spreadsheet such as Excel would suffice to enter data for most studies. Epi-Info is a free program which can be obtained from CDC Atlanta website which also helps in epidemiological data entry and analysis. If you plan to do very sophisticated analysis, perhaps data should be entered in advanced software; the catch here is that such programs are usually extremely expensive, precluding individuals from buying and using them. There are, however, freely available programs of comparable power and sophistication, such as "R"; this program needs a lot of familiarization before one can easily use it.

The advantage of many programs is that you can reproduce the proforma or protocol on the computer, so that as you open the data base, the computer prompts you with the same questions in the same order as in the questionnaire; you only have to type in the answers from the completed forms. It is useful to decide on numerical codes for most answers before you enter them, as it facilitates

analysis. Analysis software also helps you to put in checks on data entry, which reduces the number of errors. Ideally, after data entry, it should be checked randomly for wrong entry by another person. The investigator herself can do logical checks, such as looking for unlikely or illogical entries in age or sex or other characteristics. In case such entries surface, the original protocol should be verified for mistakes in data entry.

Data Presentation and Reporting

After data entry and cleaning of data, they should be examined for their distribution and patterns. This is called *data description*, and suggests clues about what further analysis to do. It may point to possible associations between variables and the outcome—these are to be further confirmed by analysis. It may bring up unusual values for some characteristics in some individuals—'outliers' or strange data. These should then be checked to see whether these are genuine values, or have come about as a result of mistaken data entry. Sometimes outliers are discarded from further analysis.

We generally use various types of charts to describe data distribution—the commonest are histograms, bar charts, line diagrams and pie diagrams. In reporting findings of a study, we should neither underplay nor exaggerate; use plain, 2 dimensional charts with clear labeling.

Relationships between two attributes in subjects are usually brought out by cross tabulation—these are presented as tables. Tables should always have a header which indicates the table number in Arabic (never in Roman) numerals, and explains what is presented in the table. Both rows and columns should be clearly labeled, and if the source of information in the table is not from the data collected by the researcher, the external source should be clearly mentioned at the bottom of the table. All tables and charts in a research report should be self-explanatory, which means that the reader should not be forced to refer back to the text to find out what the table or chart is showing. Tables should generally be devoid of all grid-lines; you may use a few horizontal lines to set off important rows such as the header row, but never use vertical grid lines.

The writing of the research report should follow the pattern set in the research proposal: *introduction, objectives, methods, results, discussion, conclusions, acknowledgments, appendices*. Introduction contains the brief review of literature and presents the case for doing the study. Next come the specific objectives for the current study, followed by the methods section. The methods should cover the population in which the study is undertaken, the method of selecting the sample, the number of subjects in the sample, inclusion and exclusion criteria for selection, design of the study, instruments used for extracting information, including study questionnaire or laboratory methods and how they were developed and validated. All tables and charts, and any other relevant findings from the study, are included in the results section. Discussion of the results should be done in the light of the earlier studies, and any limitation of the study that the author is aware of should be mentioned here. The last section should set out the salient conclusions from the study.

References should be given in the correct format. Generally, medical articles follow the Vancouver style, otherwise known as the 'uniform pattern for biomedical journals'. Here whenever a previously published work is quoted or referred to in the text of the research report, it is acknowledged by a number. This number is generally given as a superscript and follows the order in which the references appear, the first reference given the number 1, the next number 2 and so on. Each article is numbered the first time it is referred to, and any further reference to it indicated by the same number. At the end of the text, after the main body of the report, in the reference section, all the referred articles and books are listed in the order in which they are referred to, indicated by their corresponding number, with the name of the journal, year of publication, volume, and page numbers. Books, and chapters in books, also have a distinct citation style (details are given on the website: *Citing Medicine: the NLM style guide for authors, editors and publishers (www.ncbi.nlm.nih.gov)*).

Example of Reference to Journal Article

C R Soman, S Safraj, V Raman Kutty, K Vijayakumar, K Ajayan. Suicide in South India: A community based study in Kerala. Indian J Psychiatry 2009;51:261-4

Example of Reference to Chapter in a Book

Richard Doll. Development of the epidemiology of cancer. In: Holland WW, Olsen J, Flurey C V (ed), The development of modern epidemiology: personal reports from those who were there. Oxford University Press, Oxford 2007:63-69.

Examples of Data Representation: Bar Chart (Fig. 57.1)

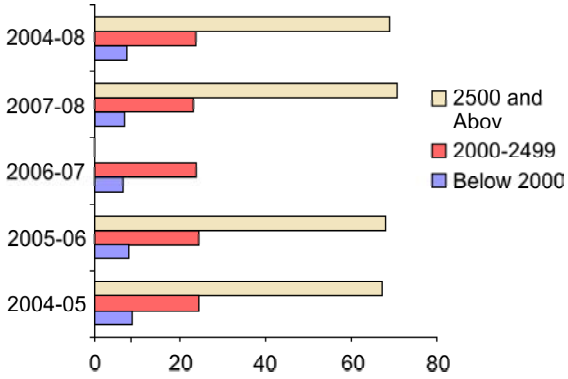


Fig. 57.1: Bar chart showing birth weight proportions, Jhagadia district, Gujarat, 2004–2008
(*Source:* SEWA-Rural Hospital, Gujarat)

Examples of Data Representation: Line Graph (Fig. 57.2)

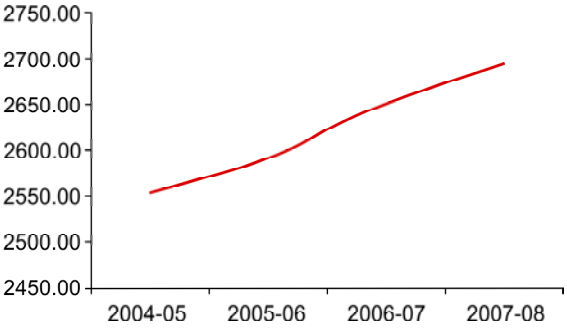


Fig. 57.2: Mean birth weight in Jhagadia district, Gujarat, 2004-2008
(*Source:* SEWA-Rural Hospital, Gujarat)

Examples of Data Representation: Pie Chart (Fig. 57.3)

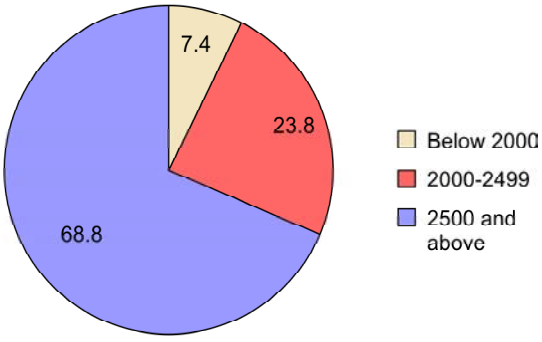


Fig. 57.3: Birth weight categories in Jhagadia district, Gujarat, 2004-2008
(*Source:* SEWA-Rural Hospital, Gujarat)

CHAPTER

58 Community Medicine

V Raman Kutty

Community health, Health status of community, Millennium development goals, National Health Policy (2002), Role of doctor in health care delivery, Primary health care, Role of a PHC doctor, Health information system, Organization of clinical practice by a young doctor, Health Education

COMMUNITY HEALTH

Over the past several decades the pattern of disease has changed. With the spread of universal immunization, improvement of sanitation and availability of various antibiotics, epidemics of infective disease began to decline. Changes in the human environment and behavior have brought in newer health problems such as increased occurrence of atherosclerotic disease, occupational diseases and intentional and unintentional injury such as accidents and homicides. Highly specialized and complex modes of health care are available in the country, but access to the most basic care is still not universal. The concept of family doctor and that of primary health care through the network of primary health centers as envisaged earlier by our policy makers has failed to take effect. Many of the medical practitioners in rural areas remain outside the mainstream of medical progress.

Social medicine is the study of man as a social being in his total environment. It includes prevention of diseases, administration of medical services and the study of the medical needs of society in addition to patient care. Its focus is on the health of the community as a whole and not just on the health of the individual in isolation.

HEALTH STATUS OF THE COMMUNITY

The main determinants of health such as adequate income, nutrition, education, sanitation, safe drinking water, and preventive and curative health care are accessible to most of the population of the developed nations, but only to some in the developing nations. Only 25 to 30% of the population in the developing countries has ready access to any type of modern health care. Medical practitioners and facilities are clustered mainly around the cities and towns. The life expectancy in the developing countries is almost 30 to 50% less than that of the developed countries, except for a few select regions. Infant mortality rate is still 60 to 80 per 1000 live births in many parts of the developing world, compared to the figure of 10 in the developed countries.

The World Health Report, 1998, published by the World Health Organization, predicted that by 2025 worldwide life expectancy at birth will reach 73 years. *Life expectancy at any stage is the additional number of years a person at that age can expect to live, provided the conditions of mortality prevailing at the time continued unchanged.* In 1955 average life expectancy at birth in the world was 48 years. There will be around 800 million people above the age of 65 by 2025, almost 10% of the total population. In the west the proportion could be much higher.

At the same time, two fifths of all deaths in the world in 1998 could be described as premature, as they were before the age of fifty. 20 million a year die before this age, though average life expectancy has risen to 68 years. Ten million of these are

children below 5 years. 3 out of 4 people in the least developed countries of the world die before the age of fifty. Two million children die every year from diseases for which there are effective vaccines. Most of these deaths occur in developing countries.

Though there has been a great improvement in health all over the world, the fruits of this achievement are not equally distributed. The rich countries have the greatest advantage. Technological progress and economic development in those countries have played a role in this. Food supply has doubled in the past 40 years, and per capita income globally has risen by 2.5 times in 50 years. Adult literacy has improved by 50% since 1970.

There has been progress in most fronts including malnutrition and infectious diseases. The world has succeeded in reducing or eradicating some of the communicable diseases. Smallpox, dracunculosis and poliomyelitis are among these. Malnutrition has been controlled in large parts of the world. However, new challenges are facing us. Chronic and degenerative diseases such as coronary heart disease, Alzheimer's vascular disease, connective tissue disorders and joint problems are on the increase worldwide. Depressive illness and psychiatric disorders have grown to almost epidemic status now. Accidents, homicides and suicides are also growing numbers. It is difficult to predict what the effect of new infectious diseases like AIDS, Ebola, Legionnaires, SARS, H1N1 influenza and other diseases will be on global health status in the 21st century. Thus, the physician of the future can expect to have a new set of challenges. He or she should prepare to meet them by developing new tools and learning new skills, while being well versed in the fundamental principles of medicine.

THE MILLENNIUM DEVELOPMENT GOALS

The Millennium Development Goals (MDGs) are eight goals to be achieved by 2015 that respond to the world's main development challenges. The MDGs are drawn from the actions and targets contained in the Millennium declaration that was adopted by 189 nations and signed by 147 heads of state and governments during the UN Millennium Summit in September, 2000.

The Eight MDGs are as follows:

Goal 1: Eradicate extreme poverty and hunger.
Goal 2: Achieve universal primary education.
Goal 3: Promote gender equality and empower women.
Goal 4: Reduce child mortality.
Goal 5: Improve maternal health.
Goal 6: Combat HIV/AIDS, malaria and other diseases.
Goal 7: Ensure environmental sustainability.
Goal 8: Develop a global partnership for development.

We can see that the MDG's are directly concerned with health; while goals 4, 5 and 6 are specific health targets, others are contributory factors. The maternal mortality, infant mortality and underfive mortality targets to be achieved by India by 2015 are: 109/100,000, 27/1000, and 41/1000 live births respectively. Though considerable progress has been made, India has not achieved the goals set for the country in the MDGs.

NATIONAL HEALTH POLICY (2002)

After the National Health Policy of 1983, a new National Health Policy was announced in 2002 which differs considerably in its orientation from the previous one. Though National Health Policy, 1983 had a grand vision of reaching health for all by 2000 though emphasis on primary health care, looking back, we see that most of the targets were unachieved. This led to a more realistic assessment of our resources and needs, which is reflected in National Health Policy, 2002 (NHP). NHP sets the following targets for the health sector in India:

1. Eradication or elimination of major infectious diseases: Polio (2005), leprosy (2005), kala-azar (2010), filariasis (2015).
2. Achieve zero growth of HIV/AIDS by 2007.
3. Achieve 50% reduction in mortality due to tuberculosis, malaria, vector born and water born disease.
4. Reduce infant mortality rate to 30/1000 and maternal mortality rate 100/1000,00.
5. Increase health expenditure by government as a percentage of gross domestic product (GDP) from the current level of <1 to 2% .
6. Increase the share of central assistance to states in the health sector to at least 25% of state health spending.
7. Increase the state sector health spending from 5.5 to 7% of the budget of the state.

To achieve a more equitable distribution of resources in the health care sector under government, NHP proposes the primary health care should receive 55% of total health spending by the state, with the secondary and tertiary sectors receiving 35% and 10% respectively. It also envisages a greater role for the local self-governments (LSGs) in planning, budgeting and running of the primary health care institutions. In the field of personnel, it emphasizes the need for correcting the imbalances in the present mixture of generalists and specialists, by creating more training opportunities for family physicians and nurses. There is also need for improving selective areas of care, such as mental health and trauma care.

The private sector plays a large role in providing care in India, a fact which governments have failed to acknowledge and continue to ignore in policy making. NHP devotes a special section to the private sector, welcoming its participation in all levels of health care. However, it sees the need for setting standards of infrastructure, equipment and training in the private sector and for monitoring its performance through a system of accreditation. The need for social health insurance to cover the poorest sections of the society, so that their spending in the private sector can be subsidized, is also envisaged.

Other areas of concern in the NHP are the cost of drugs and their availability, including the impact of globalization and the need for combating its adverse effects on the population, ethics and health research, environmental and occupational health.

Two of the most important policy initiatives to follow from the NHP are the National Rural Health Mission, and the Health Insurance Scheme for the poor. The NRHM proposes to strengthen the rural health care infrastructure in the country through providing enough resources in the public sector in health. It provides funds for appointing doctors and other personnel, as well as for developing infrastructure and for consumables. It is envisaged as a participatory program, with the local self-governments (LSGs) playing an active part. Every village is expected to form a village sanitation committee consisting of both health workers and representatives of the people, who will look after public health issues in the village. The uniqueness of the NRHM is that it functions through female health workers called ASHAs, or Accredited Social Health Activists. They are selected by the community who help in empowering the community by helping them to utilize the health programs of the government.

The social health insurance scheme covers all families who are too poor to afford health care, and provides cashless access to accredited health facilities for all such families up to an amount stipulated by the government. This recognizes the fact that in spite of government health facilities, many poor people still approach the private sector for health care. In this scheme, the government pays a premium to cover their health needs, which entitles them to a health card. This card will be honored in all accredited health institutions for provision of free health care up to a maximum stipulated amount. This scheme is implemented through the state health departments.

ROLE OF DOCTORS IN HEALTH CARE DELIVERY

Any doctor working in a community should assess its health status and health needs as an essential prerequisite. The health problems may vary from place to place and in different communities depending on the lifestyle and other characteristics. Major contributing factors to the health problems in India are:

1. Communicable diseases.
2. Malnutrition.
3. Inadequate sanitation.
4. Inadequate medical care.
5. Population explosion.

The Government of India has launched various national programs from time to time to tackle these problems.

The main national programs having a bearing on the health are:

1. Malaria eradication.
2. Filariasis control.
3. Tuberculosis control.
4. Leprosy eradication.
5. Diarrheal disease control.
6. Sexually transmitted diseases (STDs) control.
7. Prevention of blindness and visual impairment.
8. Control of iodine deficiency disorders.
9. Universal immunization.

10. Family welfare.
11. Water supply and sanitation.
12. Guinea worm eradication.
13. Diabetes control.
14. Control of acquired immuno-deficiency syndrome (AIDS).

Most of these national programs are implemented through the primary health centers (PHCs) whose medical officers are the key persons responsible for implementation.

PRIMARY HEALTH CARE

The concept of primary health care (PHC) was originally conceived at an international conference at Alma Ata in the former Soviet Union in 1978. Elements of the same idea was contained in the recommendations of the Bhore committee report which was published in 1946. Primary health care was conceived as a strategy for achieving health for all by 2000. The components incorporated in PHC include:

a. Education about prevailing health problems and methods to prevent and control them
b. Promotion of food supply and proper nutrition
c. Adequate supply of safe water and basic sanitation
d. Maternal and child health care
e. Immunization against infectious disease
f. Prevention and control of locally endemic disease
g. Appropriate treatment of common diseases and injuries and
h. Provision of essential drugs. The PHC approach is based on social equity, universal coverage, self-reliance, intersectoral co-operation and peoples' participation indecision making.

For the physician, the PHC philosophy should form the cornerstone of practice. It is essential to think of disease in the context of the social, cultural, and economic situation of the family. The physician should be concerned not only with diagnosis and treatment of the individual patient, but should try to learn about the family background, the paying capacity, the level of understanding and the consequences of disease for the family. He should counsel the family members on the proper support and care for the patient. Health education leading to preventive and promotive aspects should form a part of the doctor's advice. The doctor should also be aware of the national programs for control of diseases, and where service is available for the patient. The doctor should also carefully keep the records of the patient for further references.

In India, primary health centers, or PHCs and their subcenters form the first accessible health care institution for the rural population. Only those needing higher level care are to be referred to larger hospitals. The orderly delivery of health care through this network of primary, secondary and tertiary care centers along with preventive and promotive activities is what is conceived as primary health care. Primary health care, however, is not limited to PHCs; it is delivered through a much wider network including private general practitioners and private hospitals. Much of the work of the outpatient departments of major hospitals also involves elements of primary health care. Ideally, primary health care should incorporate the principles of:

i. *Continuity of care* (the same physician sees the patient in the first instance in every episode of illness, and in the event of hospitalization, the patient is sent back to the primary care physician after discharge).
ii. *Comprehensive care* (a patient goes to the same physician first whatever be the nature of the complaint, and is referred to a specialist by the primary care physician if necessary; an arrangement technically known as 'gate keeping').
iii. *Patient choice* (patient should be able to choose which physician he/she will go to in case there is an illness).
iv. *Total coverage* (everyone should have access to primary care irrespective of their ability to pay). For this, building up a long lasting relationship between doctor and patient is essential. On the other hand, secondary and tertiary care (based in hospitals), involves team work involving the doctor, nurse, other health workers, and paramedical staff, and does not depend on the doctor alone.

Primary Health Centers

In India Primary Health Centers (PHCs) were established in 1952. PHC is the peripheral health institution provided with a team of medical and paramedical staff through which several health programs are implemented. PHCs were originally started as part of the community development programs for a population of 1,00,000 living in a

defined geographical area. Subsequently several modifications have occurred. At present mini PHCs have also been established and therefore one PHC serves a population of 30,000 only. The PHCs undertake comprehensive health care including preventive, promotive and curative services. There is a subcenter for a population of 5000.

ROLE OF A PHC DOCTOR

The medical officer is the leader of the health team. In addition to his clinical responsibilities he has to perform other duties. He should have communication skills to educate and motivate his staff to do their jobs effectively. The medical officer of the PHC is responsible for all health related events occurring in his area. This includes epidemiological investigation and preventive action when outbreaks of diseases occur. His skills should include management of the six M's viz. men, materials, machines, money, methods, and moments (time). He could be conversant with the basic principle various health data available to him, and for onward transmission.

The PHC doctor should have clinical skills to impart curative services in a situation where many laboratory tests and other sophisticated investigations may not be available. He should refer patients in the right time to higher centers for further management. The doctor should realize the limitations in imparting curative services in the rural set up. The vast majority of the health problems encountered in a primary health center can be managed there itself if the doctor applies his skill and judgment effectively. He should establish proper liason with hospitals where specialist care is available. Once the patient comes back from these centers, the PHC doctor should continue further management and follow-up.

HEALTH INFORMATION SYSTEM

For the effective practice of medicine, a physician needs a continuous flow of information. The organization and storage of health records should begin with the primary care physician. He or she needs to be up to date on the latest developments in the research front, especially the current management of common diseases. For this the physician has to depend on a variety of sources. Information is essential also for managing a hospital or doing research. Thus the quality of medical care depends to a large extent on the quality of health information. Information should be *current, reliable, explicit, relevant, readily available*, and in a form which could be used easily. Depending on the type of information needed, the sources vary.

For information on the health status of communities, physicians can make use of the following sources:

Mortality and Fertility Statistics

These include the *crude death rate,* the *crude birth rate,* the *infant mortality rate, maternal mortality rate,* and the *fertility indices.* These are available from sources such as the census reports, the sample registration system of the Government of India, and other publications of the ministry of health.

Morbidity and Utilization Statistics

Morbidity refers to the level of sickness. Among statistics relating to morbidity will be prevalence and incidence rates of various diseases, number of work days lost due to disease. Utilization statistics refers to information on the use of the health system by the people. Rates of hospitalization, people's preference for various systems, and public versus private hospitals estimates of money spent on treating sickness, proportion of births in hospitals, immunization coverage, all belong to this class of statistics. These are not routinely collected in India. They may be available from various surveys. The National Sample Survey Organization and the National Council for Applied Economic Research (NCAER) are two organizations which occassionally do such surveys.

Practicing physicians may have much more need for information regarding current development in the understanding and management of diseases in their speciality. For this they traditionally have depended on a variety of sources such as journals and textbooks. Now they have a wider choice of sources including the Internet. However, all sources may not guarantee the same degree of authenticity in the information they provide. The major such sources are:

a. *Continuing medical education programs:* These have become very popular. The reliability of the information provided is dependent to a large degree on the speaker. Hence it is worthwhile checking the credentials of the person providing the information before accepting it.

b. *Textbooks:* Textbooks are generally a reliable source of information, as a fair amount of planning and editing go into their preparation. The one drawback with text books as a source of knew knowledge is that they tend to be slightly outdated. This is because the preparation or revision of large volumes take time. Recently, developments in printing technology using the computer have made the process much faster, hence this may no longer pose a serious problem.

c. *Journal articles:* Journal articles continue to provide very current information for the clinician. Among journal articles, review articles are the most authentic since they collate a lot of facts from multiple sources. Original research articles report findings of a single research group. The information they provide can be incorporated into practice only with some caution. It may always be better to wait till a new finding is corroborated by other independent researchers.

Among journals, peer reviewed journals which are indexed in the cumulated index medicus, medline, excerpta medica or any other indexing service are the most reliable. This is because a journal has to attain certain standards in editing and publicaion before it is accepted by the indexing service. A list of journals which are indexed will be available from any good library.

A general medical journal such as The Lancet, British Medical Journal or New England Journal of Medicine should always be rated higher than a speciality journal. A general medical journal accepts articles which are of interest to all the medical community. These are likely to have a greater impact on current practice. Speciailty journals may report articles which are more of theoretical interest to those in the speciality.

d. *The worldwide web:* The latest development in information technology which is relevant to the practicing doctor is the internet or the worldwide web. This is a global network of computers which can be reached through telephone lines and satelites using a personal computer in the home or office. Several sites on the web offer medical information. Unfortunately, not everything present on the web can be accepted as authentic. Medline which is the collection of all abstracts from over 3000 current journals produced by the national library of medicine (NLM), USA, is the best source of medical information on the internet. Medline is available at several sites on the worldwide web including the sites of leading journals such as the Lancet, BMJ, NEJM, etc. special interest groups related to various practicing specialities which are present on the web provide another quick way of being abreast of current developments in the field.

ORGANIZATION OF CLINICAL PRACTICE BY A YOUNG DOCTOR

Knowledge of a few principles of management will enable a doctor to develop his on clinical practices at various levels. A general outline is given below:

In a clinic the doctor is the manager. He should be able to organize and implement his practice effectively applying managerial skills.

Man Power

Managing men is the most important aspect. Different type of people with different attitudes, ways of living and different educational background approach the doctor for health care. A knowledge of human psychology, empathy and tactics are essential for managing the people.

The staff or subordinates working under him should be properly taken care of. Their defects and deficiencies should be corrected. They should be motivated, guided and supervised properly. Their exact nature of work and its implication on the general outcome of the practice should be made known to them. Encouragement and emotional support should be provided whenever necessary, in order to improve their efficiency and motivation.

Money, Materials and Machines

The available resources should be effectively utilized. The doctor should set out with a clear idea about the type practice of hospital he would like to have developed. The place which he is going to select should be suitable to practicing his specialty. The local conditions and situation should be taken into consideration before investing money.

Preliminary survey of the health condition in the area and a few contact sessions in order to acquaint himself with the local inhabitants will go a long way to establish himself in the community.

Materials and equipment should be procured based on the need. The utility and cost benefit ratio should be taken into consideration while ordering equipment such as ECG, X-ray machine, ultrasonographs, laboratories and others.

Time

The patient's time is equally important as that of the doctor. Managing time is another important aspect. Time for individual consultation, duration of hospital stay, waiting time, and frequency of consultation, should be carefully planned. Proper clinical examination, basic investigation and formulation of a provisional diagnosis are all important in instituting early treatment. There should also be a proper system for specialist consultation and referral to higher centers.

Interpersonal Skills

Though the practice of medicine is primarily concerned with understanding patient's problems and finding solace for them, there is a general concern that doctor's skills in the area of communicating with patients and comprehension of their issues are not as keen as they used to be a generation ago. There could be several reasons for this. For one, the growth of technological sophistication forces young doctors to spent a great amount of time mastering varied technical skills. This leaves them little time for consciously developing their ability to interact with patients. The explosive growth of specialization has contributed to this. Formerly the personal element in the doctor's manners, the ability to soothe the patient's feelings and inspire confidence by his or her behavior was a large component in what the physician gave to each patient. The purely technical content was much less important partly because therapeutic science had not advanced so much. Now there seems to be a reversal of the situation. With the advance of treatment of modalities and their variety, the personal element in doctor's behavior has assumed a less important role, especially in the doctor's minds. Modern medical training also contributes to this by laying less emphasis in developing interpersonal skills. In many medical schools, these may never be assessed at any point and a student who has high degree of competence in this area may go unrewarded.

Doctors interact with patients in many situations: in the clinic, in the ward, prior to surgery, and post-operatively. There are also many different occasions which demand different approaches to handling. The doctor may be called upon to convey the diagnosis of a fatal disease to the patient or relatives. He may have to gently guide the patient and family in a difficult decision. The patient any seek his guidance in coping with a chronic disease. In any such circumstance, the following guidelines may help:

1. *Be honest:* There is nothing to be gained by offering false hopes. Though the patient or relative may be upset at first, he or she soon realizes that you have helped to make a better decision by being honest.
2. *Be gentle:* Even the worst diagnosis can be conveyed with empathy and understanding; the doctor is in a better position to deliver this than any other health worker.
3. *Be understanding:* Remember that the patient and relatives in a clinic or hospital setting are in an intimidating environment, and quite likely to be under great stress. They may behave in a less than pleasing manner; it is not for the doctor to react.
4. *Be efficient:* Do not contribute consciously to the wastage of the patient's time or resources.
5. *Be open:* Discuss all options with the patient or relative, and if they desire a second opinion or consultation, encourage this.
6. *Be deliberate:* Above all, spend time with the patient. Discuss his or her problems, even if they do not relate immediately to the sickness.

HEALTH EDUCATION

This aims at inducing changes in personal and groups attitudes and behavior so as to promote healthier living.

The main objectives are:

a. Informing people
b. Motivating people
c. Guiding them into action.

Practice of Health Education

1. *Individual and family health education:* A doctor has a major role in health education in his clinic or consultation room. Educate the person on matters of health such as diet, causation and nature of his illness, methods for prevention, personal hygiene, and others. By this, the individual and family will be equipped to tackle their health problems more effectively.
2. *Group health education:* Matters of health directly important to the group have to be introduced and discussed in camps or seminars, e.g. feeding practices to the mothers, immunization to children.
3. Educating of the general public through mass media like television, radio, newspapers, and magazines. Health education message can be disseminated widely.

SECTION

21

Information Systems in Medicine

CHAPTER

59

Practical Applications of Information Technology for Patient Care

KK Krishna Kumar

Information technology, Computer hardware, Software organization, System architecture, Internet and world-wide web, Selection of IT systems, Biomedical equipment and electronic accessories, Practical applications of IT in health care, Office automation and hospital, Digital library and information on the web, Decision support and expert systems, CME and collaboration, Glossary

INTRODUCTION

Information technology (IT) is now widely used by students as a valuable learning resource and easy reference facility. Medical practitioners and health care delivery institutions employ IT to automate routine administration and patient management functions. Researchers depend upon IT infrastructure to collect and process data, undertake scientific analysis, publish and collaborate with peers.

A basic IT system has to perform the end to end task of capturing information, storing, retrieving and processing, sharing and communicating through proper and secure channels. Computer manufacturers have evolved designs and specifications that support high speed data processing capability, standard digital communication interfaces and compatibility with every other equipment and accessories. Different software applications have adopted many common standard features, intuitive displays with easy to understand interactive screen layout, menus and commands and context sensitive help to enable ordinary users get familiar with computers quickly. Medical professionals can purchase new computers off the shelf and straight away put it to personal use, with a little hand on training and some technical help.

However, the know-how required connecting personal computer (PC) to a network through a port or set up a terminal as part of a network is a specialist's job. Only a certified network professional or system administrator can create unique network identity (ID), set up user rights and access control, partition the hard disk for shared and nonshared files, provide data backup drives, configure separate protocols for communicating through private and public networks, create priority queues for different devices connected to the network like internet gateway, e-mail servers, DVD/CD drives, printers, scanners, fax and public information displays and install firewall and antivirus software and periodically audit the network for security risks. The infrastructure required to support any information system is made up of computers, communication devices, institutional data networks, shared network, internet access gateway and a variety of software. It is now more often described as *information and communication technology* (ICT). Today the industry standard computer hardware and software are configured to plug-n-play when connected to existing system.

Information is value added data: Text content and pictures (graphics) which has been formatted, cross-referenced, captioned and hyperlinked (to original source) is the first step in storing a digital record or electronic document. Numbers, ranks and grades and logical (Yes or No) attributes can be sorted, filtered, summarized or mathematically and statistically analyzed. Processed information is used for monitoring, comparing, inferring and decision

making. Processing electronic medical records includes:

i. Collection and systematic storage of data.
ii. Compilation and update of data recorded at different time intervals (date).
iii. Conditional or selective retrieval of data and creating need based reports.
iv. Comparison of observed data to normal parameters.
v. Numerical analysis and reviewing evidence before decision making.
vi. Data mining and developing expert systems.

Hospital management systems are enterprise wide solutions that integrate patient information, record of clinical and paramedical services, workflow administration, resource management and financial accounting. There are cost effective solutions to manage operations of any scale from consulting chamber practice to multispeciality hospitals.

IT can collate, correlate and combine data obtained from different sources, both qualitative (like radiologist's opinion) as well as quantitative (like lab report) and assist doctors in decision making. Automation of diagnostic services improves reliability, staff productivity and patient satisfaction. Computer controlled instruments and equipment relieve health care professionals of routine tasks and repetitive procedures which are prone to human errors. Lab quality control measures can be implemented through computerized records audit. Web and mobile phone enabled applications help patients schedule appointments, check follow-up visits, send lab reports and seek medical advice without contacting the administrative personnel in a clinic or hospital. Doctors offer professional assistance to remote clinics and individuals through telemedicine.

COMPUTER HARDWARE

Practically every application in medicine can be run on *desktop* or *laptop* computers. The data processing speed of the central processing unit (CPU) is determined by the specifications of the chip manufacturer (Intel, AMD, Motorola or Cyrix), quality of the motherboard and the clock speed in mega /giga hertz. It is important to install adequate random access memory (RAM) according to the minimum RAM recommended for installed software applications. Providing additional RAM capacity will improve performance when handling big file size, multitasking, online information sharing and sending and receiving video, audio and high resolution images through broadband connections. The display monitor, hard disk drive, CD/DVD drives keyboard and mouse forms part of the basic equipment. Software requiring high performance computing like Holter signal analysis, pacemaker activity monitor and digital image processing (DICOM standard) calls for hardware upgrade like extra RAM, additional external cache memory, graphics accelerator cards and high performance hard drives instead of standard ones. Personal computers should also have additional ports/ expansion slots to connect add-on devices when necessary, like external speakers, MP3 players, pen drive, portable hard disk, webcam, projector, video recorder, digital camera, mobile phones and to directly plug in flash memory cards. Therefore serious users should look for expansion slots like audio and microphone jack, USB ports, VGA output, PS/2 connectors, PCMCIA ports or card reader, ethernet port (RJ45), phone jack (RJ11), Firewire/ IEEE 1394 port and HDMI (high definition multimedia interface). Sometimes if you have to connect the computer to old type of analog projectors or television and printers or scanners the S-Video connector and Parallel ports should also be included. Most laptops are equipped with built-in wireless LAN adapter for accessing Wi-Fi hot spots, 3G/ WiMax for mobile phone services, Bluetooth for close range device to device data transfer and IR remote control (Figs 59.1 and 59.2).

Nowadays, a standard desktop or laptop having Inter Core 2 Duo 2.1 GHz processor, 15" TFT-LCD monitor of XGA resolution, 2 GB RAM, 200 GB hard disk capacity and other standard specifications



Fig. 59.1: Laptop computer



Fig. 59.2: Desktop computers connected in LAN

and accessories should be adequate for medical professionals. Desktops are less expensive, more comfortable to operate, delivers better performance and easy and cheaper to upgrade. Laptops consume less power with long duration battery backup, are rugged and shock proof, light weight and portable. Desktops are best suited for routine professional and office work and Laptops are only for people on the move.

Personal computers have evolved from two popular design standards—IBM compatibles or PCs and Apple macs. Though IBM brand personal computers business was sold off to another company, their innovations continue to influence new generation machines.

SOFTWARE ORGANIZATION

Computer users only know English like or similar spoken language commands to make systems work. However these commands have to be translated into equivalent set of electronic instructions (machine language) for the hardware to process. Step by step instructions that translate a user's command into machine language to process a set of input and display the output in a readable form is called a computer program. Several programs that function together to execute useful real life tasks is called software. Hardware is not functional without the instructional logic, i.e. software. Software is classified according to its control hierarchy and scope of operation.

Operating System

The hardware is assembled using components or modules that are dedicated to perform one or at times few important tasks only. Each module has built in, unerasable (hard wired) instruction set to process inputs according to predefined logic. This is known as default conditions or standard routine logic that comes with factory settings. However for any practical use these hardware modules have to be configured or readjusted according to each one's personal needs. The software that directly interacts with hardware (low level program) through simple one step at a time instructions is called operating system (OS). Operating system configures the operation of each hardware component, manages the data communication between components, prevents fatal errors and data loss and acts as an interface between CPU and higher order software features (high level software). When a computer is switched on, the most essential instructions of the OS stored in the hard disk is automatically copied to the protected address area of the RAM. This 'booting' has to proceed uninterrupted before the computer can respond to user commands. After booting the system is ready to receive external inputs and commands and the OS layer co-ordinates the job scheduling on each component (module), manages memory access, maintains internal communication pathways, synchronizes data flow and diagnose and rectify errors to complete the given task.

Personal computers with earlier OS like CP/M, DOS are rarely found these days. The popular OS for personal computers are Microsoft WINDOWS, LINUX and Apple Mac OS. A network OS allows sharing of files and resources like printer, scanner across a local area network or intranet. Many institutions still maintain client/server and peer-to-peer type of networks running Microsoft WINDOWS NT or some version of UNIX, Sun Solaris or Novell Netware on their user terminals for accessing storage area networks (an array of hard disks) and high speed and secure connections, with much less likelihood of crash when compared to PC OS. Increasingly with more and more Web applications being developed that uses the ubiquitous TCP/IP communication protocol, all personal computer OS will be able to access any type of network servers (high performance computers) and shared devices in a network without network OS. OS does not come with any ready to use medical applications. It features only

housekeeping tasks like configuring the look and feel of user interfaces, configuring devices, data security and access control, hard disk access, file and folder organization and error diagnostics, fault fixing and data recovery. Before buying a computer with preinstalled OS or when upgrading to a new version or when changing to a new OS, users have to make sure that the utilities and application software they wish to run subsequently is compatible with it.

Utility Tools

Software that provides short cuts to make routine tasks easier, enhances system performance, improves security and guarantees virus protection, and helps recover from data loss, software corruption or system crash is known as *utility*. Utility software sold by third party vendors are more user friendly and technically superior to similar features available in the OS itself. Popular utilities include system recovery manager, disk storage and clean up, file sharing, data compression and encryption, Antivirus and performance enhancing tools.

Programming Language and Software Development Kit

Programs written in English like vocabulary follow a set of rules—program syntax. But the hardware can only process digital signals that represent instructions in binary codes (combination of 1s and 0s). Language processors convert programs written using English like commands into machine language. COBOL, FORTRAN, C, C ++, HTML, SQL and Java are popular programming languages.

A computer program is only part of software. A program is first created without syntax errors, in an easily understandable format after inserting suitable comments with a text editor. It is run in a controlled manner, tested for errors (bugs) in response to different data input conditions, and then the bugs have to be traced to the particular line of code in the program and fixed. After a piece of program code is error free, it is compiled together with other programs to generate the software. Whenever there are changes in the software code the development team has to keep track of the all previous versions so that an earlier version can be restored, in case the latest release has major bugs. In order to speed up the software development project many library functions or sub-programs of frequently used instruction set are maintained and reused by simply linking it to any new program which is under development. Thus, software professionals make use of an integrated development environment that comprises of source code text editor, run time simulation, testing and debugging platform, compiler or interpreter, version control and build automation tools to deliver application software packages. Microsoft visual studio, Java development kit and Microsoft. Net Framework (pronounced dot net) are popular application software development tools (Figs 59.3 and 59.4).

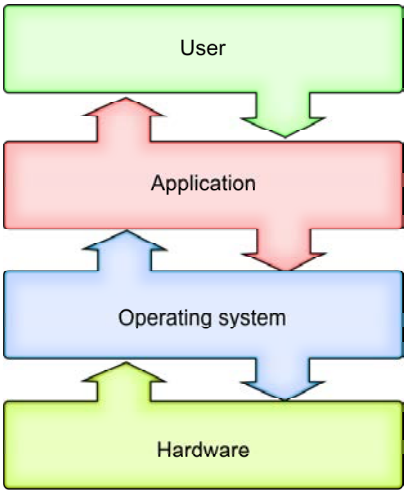


Fig. 59.3: Different software layers

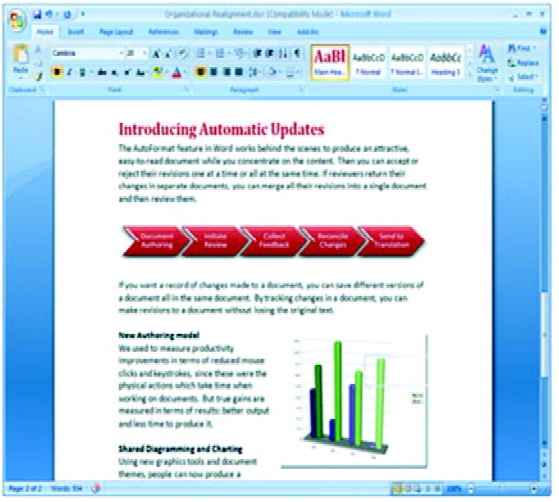


Fig. 59.4: Standard view of word processor

Business and Enterprise Application Packages

First time computer users should learn to work with the basic features of PC software like office automation package, personal organizer, e-mail, internet browsing, virus scanning and easy to use photo and graphics editing software before attempting to work with feature rich enterprise software and web applications. The office automation software consisting of a word processor, spreadsheet, slide presentation and optionally a database should help beginners handle digital information. There are several commercially off the shelf (COTS) packages for PC applications. Microsoft office, corel word perfect office and IBM lotus symphony are widely used office automation tools. Adobe illustrator, coreldraw and adobe photoshop are software applications for graphics and photo editing tasks. Norton, McAfee, Kaspersky and K7 are leading brands in antivirus software. Software protected by copyrights has to be licensed for use. The license fee for personal and home use editions of popular branded software is reasonable and ensures technical support and regular upgrades from the company.

Free and open source software (FOSS) that can be used without such copyright restrictions are also available in lieu of proprietary software. It can be downloaded from official websites and installed either free or for a nominal fee. OpenOffice.org is an office suite which is the most widely used FOSS application. It originated as StarOffice and today mega corporations like oracle are offering their versions of FOSS. However, users may have to depend upon independent software professionals and third parties for technical support and training. Before a particular version of an OS is installed or upgraded make sure that the existing application software is compatible with it.

Buying or custom made business application software or enterprise solution is a joint effort by a team of system analysts, software developers and end users. System analysts are consultants who have the domain knowledge about clinical practice, health care delivery processes and hospital administration and are familiar about the technology, software project management and cost. A hospital information system integrates administrative, financial and clinical aspects of the hospital. Key functional areas it can support are:

- *Patient administration:* Front office and inquiry counter, patient registration, appointment scheduling, duty rosters, bed allocation and medical records archive, public relations and customer relationship management.
- *Patient care:* Attending doctor's notes, instructions and prescriptions, ward notes, nursing station circulars and bulletins, EMR.
- *Clinical support:* Interventional procedures, diagnostics center and laboratory, imaging center, OT services, pharmacy, blood bank.
- *Business support:* Quality audit, utility services, materials management, contractors and outsourced service providers accounts, HR and payroll, financial accounting and corporate communications.
- *Revenue management:* Billing and collections, doctor's fees, medical insurance and claims management.

Both COTS and standard customized packages come with detailed instructions for installation and configuration and system administration guide, user manuals and demo or self-learning CD. Independent software vendors also provide 24 × 7 help desk, bug fix and technical support. In case of three tier architecture web applications, on receiving customer complaint, the software company can directly access the remote site where the application is hosted and fix any bugs without traveling onsite.

SYSTEM ARCHITECTURE

The design of software and communication protocols to meet the computing demands, network traffic and user load on a system is called architecture. During the early period in mid 80s application software was built around the database whereby the user could directly access the data, lock the files, perform useful tasks and then unlock. This one tier model became a big bottleneck when different users wanted to share the same data and system was busy processing too many user requests to respond quickly. Even today a system designed to run on a PC with one user having all privileges is called a stand alone application. Later the database was delinked from the front end (presentation for user interaction) in a client/server two tier model. In this type of multiuser system the database was maintained in the central server and only the front end ran in the client machine. Therefore the software

could automatically queue the request from the user and retrieve information from the database much faster. A client/server architecture requires a private (dedicated) network for high performance. Current three-tier application software has separate front end, business logic layer and database, all communicating seamlessly to deliver quick response. A user interacts only with the system front end. The inputs received through the front end are processed in the business logic layer and returned as output display or error messages. Data is stored and retrieved from the database only upon request by the business logic layer. The main advantage of three-tier architecture is that it is possible to provide a rich (user friendly) presentation interface without compromising speed and easy to debug and upgrade. It can operate securely across the internet (shared network) without performance issues.

INTERNET AND WORLDWIDE WEB

Medical professionals are familiar with new age phrases like 'cyber space', 'e-mail', 'web surfing', 'information super highway' and 'broadband services'. Even if these terms are unfamiliar, one sitting before a computer connected to internet can bring up a search engine like Google, Yahoo or Altavista and type in the keywords and quickly get a list of hyperlinks to dictionary, article or web page that explains the term, in a matter of minutes. The terms *internet* and *Worldwide web* (www) are often used in everyday speech without much distinction. However, the internet and the worldwide web are not one and the same. The internet is a global data communications system. It is a hardware and software infrastructure that provides connectivity between computers. In contrast, the web is one of the services communicated via the Internet. It is a collection of interconnected documents and other resources, linked by hyperlinks and URLs (uniform resource locator) (Figs 59.5 and 59.6).

The connection that allows computers to communicate, share files and access common devices is called a network. A network should have high bandwidth to carry all signals (traffic), must be secure and support industry standard connectors and ports. When the network cables are installed within a building or premises it is a local area network. A private network across different premises, states or countries using telecommunication link



Fig. 59.5: A website home page

(telephone line, satellite, optic fiber cables) is a wide area network. Interconnecting thousands of such networks through a common communication language (protocol) TCP/IP is the internet. The body of information published as text, graphic and multimedia content in public domain (free to use) made available through internet is www. A service that relies solely on its own secure network without alternate internet access is an online service. There are online services that provide value added content on payment. Users should note that:

- Online services are usually billed 'pay as you use' while internet services are fixed fee subscriptions.
- Online services exert more control on the content published and undertake editorial and peer review while internet content or www may not meet the strict academic and research standards.
- Internet can at best be a quick reference for popular topics and personal reports but good online services and e-journals should be referred for any serious professional or research work.

Before the arrival of internet, each organization could set up its own wide area network by installing routers, link directly to communication satellites through VSAT or subscribe to proprietary online services and complete the last mile through leased telephone lines. Until the internet infrastructure of servers and routers communicating across TCP/IP protocol became reliable and affordable to everyone, there were proprietary online services like AOL and CompuServ.

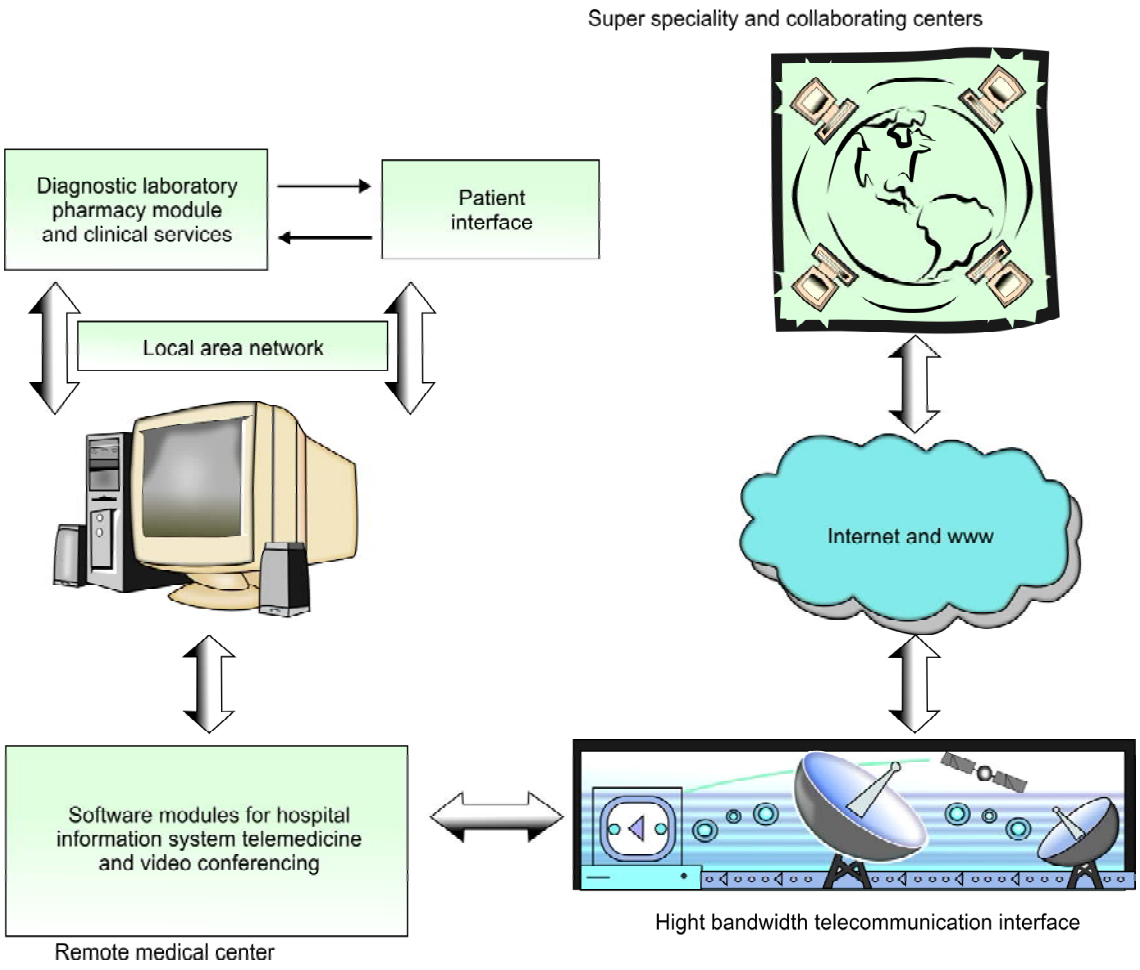


Fig. 59.6: A telemedicine network

A web browser is an application that can search and present information identified by URL from the web. Internet Explorer, Mozilla FireFox and Opera are common web browsers. An application that is hosted in a browser controlled environment and programmed in browser supported language is called web application. Web applications require very little disk space in the client, upgrade automatically with new features and is compatible with all popular OS like Windows, Mac and Linux.

SELECTION OF IT SYSTEMS

IT has a number of applications that automate the workflow processes in an institution. Introducing new systems in an environment with well established manual operations is a difficult first step. Corporate policy, peer pressure and computer literacy among staff play an important role in the success or failure of IT. The initial project should always aim to demonstrate the advantages of well designed and uniform data entry forms and quick response of the database. Gradually the manual data entry should give way to automatic data reading and display devices like attendance recording (magnetic strip), bar code readers (optical readers) and radiofrequency identification tags. Thus the system will evolve into semiautomated or fully automated solution as the organization grows.

Before investing in IT the doctor or end user and systems analyst have to evaluate the technology and features best suited for the system, cost, ease of implementation and return on investment. They have to look for *compatibility* between hardware and software, scalability without huge additional

investment, *portability* (common interface) across other electronic and biomedical equipment and open standards instead of proprietary technology. Since there are different CPUs, hardware architecture and OSs, application software packages have to be written to run across different platforms. For example among PCs running Microsoft Windows, Linux or Mac OS, each requires different set of compatible software. Sometimes two software cannot run simultaneously. It is a recommended practice to install a demo version of the software that the user intends to buy, run and evaluate its suitability before buying licensed installation.

The hardware specifications should have enough capacity to scale up (operate without loss of performance) when more number of users are added, more software is run concurrently and new electronic and biomedical devices are added and large volume of data has to be stored. The network bandwidth should be able to carry large sized images, video and multimedia files. The software should be designed on industry standard platform.

Some of the rapid application development tools or graphical user interface (GUI) for IBM compatible PC software are Microsoft Visual Basic, Java, C# (pronounced C sharp) and Embarcadero Delphi and makes use of MS-Access or MySQL database. Applications can be developed using FireWire SDK, XCode or Eclipse for Apple Mac OS. Such a system will serve the needs of a doctor or polyclinic handling about 200 outpatients a day.

Besides the simple GUIs, the popular HTML/XML standard (compatible with popular web browsers) front end tools for the rich look and feel of client/server software are PowerBuilder, Adobe Dreamweaver, Microsoft Front Page and Expression Web, PHP and similar packages. The popular databases recommended for installations with 10 concurrent users (between 50 to 200 connected users) are MySQL and lite (scaled down) versions of Microsoft SQL Server, Oracle and Sybase. Two-tier systems are adequate for a 100 bedded hospital with limited clinical and nonclinical services and offline internet access with other centers.

A large multispecialty hospital with online collaboration with other centers must have three-tier architecture systems. Many applications are developed using. NET or J2EE framework with robust middleware products and high end databases like Microsoft SQL server, Oracle, Sybase, DB2 and Informix.

While evaluating different solutions it is standard practice to compute the total cost of ownership over three years. The budget for initial implementation should include cost of hardware, communication devices and licensed software for both COTS and application software, customization of features, providing network connectivity, site installation, training and technical support. The recurring expenditure covers annual maintenance contract, upgrading licence for more number of users and consulting fees for providing technical help when new features have to be added, or new office automation equipment or hospital equipment has to be installed. Today many high end systems are available for use as software as a service model, whereby the customer is charged on a subscription plus transaction fee basis instead of one time investment. In order to compute the return on investment the project team has to take into consideration the need to modernize hospital administration and financial transactions, value addition due to improved quality of medical services, increased revenues by increasing the productivity of different profit centers and hospital staff, cost savings due to reduced administrative work and opportunities for collaboration with other doctors, outsourced service providers and hospitals.

It is less important to select systems on the basis of ease of implementation because leading computerized systems offer similar technology compatible with health care industry standards, guarantee enterprise wide integration and offer many user friendly features. It may be helpful to take a look of the feature list, installation guide, and user manuals and help files to make sure that customer documentation is of good quality before choosing appropriate software. It is more important to review the readiness of the Doctor or institution to adapt to a new system. Once the hardware and network infrastructure are in place, then the end user readiness can be understood from their awareness about the work flow process changes and benefits of new IT system, computer literacy and willingness to undergo training.

BIOMEDICAL EQUIPMENT AND ELECTRONIC COMPUTER ACCESSORIES

All new generation diagnostic, imaging and therapeutic equipment have embedded computer chips. It is important to make sure if these equipment can be directly instructed and controlled by a PC through standard input port and results, images, video or other output can be sent back through standard output port. Any information that goes into electronic medical record should be processed, stored and retrieved in file formats compatible with popular PC software. The prescribed standards are ASCII and XML for text documents (clinical document architecture), DICOM for images, HISA for general clinical information and HL7 for inter-operability with specialities. The digital images have an advantage that if the picture quality or resolution makes interpretation difficult, then it can be improved by image processing software without another repeat scan procedure. Software can also change view angle (aperture), obtain a calibrated measure of artefacts or shadows and color code according to predefined parameters. Wherever communication has to be established between the equipment and office computer without staff intervention, sophisticated accessories are interfaced.

Direct on-line EKG and EEG recording consists of leads connected to analog-to-digital converter which converts the electrical activity into digital video files which can be directly viewed on VDU or replayed later on media player software. These have done away with paper strip recordings. Remote monitoring of vital parameters of ambulatory patients through radio transmitters, wireless infrared transceivers or mobile SMS/MMS enabled gadgets are more reliable and convenient. In modern clinics and hospitals wireless hot spots are installed in several locations so that ambulatory patients are never out of range.

Ultrasonography is aided by acoustic transducers and associated circuits that can be controlled by PCs to focus, scan and reproduce echograms.

Another useful accessory is the touch sensitive graphic display screen with or without stylus. It is frequently used for web conferencing and Continuing medical education (CME) workshops for discussing anatomic details, obtaining expert opinion and planning surgical procedures.

An expensive system comprising of very high resolution 3-D display mask, high fidelity audio earphones, remote control gloves and touch force sensors are used for virtual reality simulation. Together with advanced training software, it will be used in future to train surgeons, paramedics and emergency room attendants faced with life-like situations instead of present day passive dummies.

PRACTICAL APPLICATIONS OF IT IN HEALTH CARE

Office Automation and Hospital Management

A set of office automation and personal organizer software will vastly change the way one manages information and doctors will have to devote much less time for nonclinical work. Utilities to send, receive and organize files from digital sound and video devices like webcam, close range wireless equipment, mobile phones and mobile internet connectivity will be very convenient and enhance the user experience of PCs.

Small clinics and hospitals can use COTS solutions for registration, patient records, lab, pharmacy, purchasing and stores, payroll and financial accounting. Web applications makes it easy to send and receive information that should be shared with collaborating centers like test request forms or reference letter, lab and radiology reports, prescriptions and treatment notes and discharge summary. Complete hospital information system for bigger hospitals will need some customization before it is ready for roll out. New generation ERP (enterprise resource planning) software aims to enable a 'paperless office' where all internal and external information flow is managed by the system. This facilitates easy processing of bill (receivables and payables) settlements, corporate reimbursements, insurance claims and other key business transactions.

Medical Records and Lab Automation

Patient records and case sheets are vital information that doctors have to maintain in a systematic and easily retrievable manner. The responsibility of the doctor and hospital administration as the custodian of correct, relevant, updated, and medicolegally sustainable information about patients under their care has to be emphasized while using IT for medical

record keeping. Different institutions follow different formats of medical records. The HIPAA legislation (Health Insurance Portability and Accountability Act) enacted by US Congress in 1996 laid down standards for disclosure of health care transactions, privacy of health data and administrative simplification for health maintenance organizations. Today the Problem Oriented Medical Records (POMR) template which came about as a result of the evidence based medicine principle have been incorporated in several versions of EMR. The flow of information in case of inpatients will systematically corelate history, clinical findings and general investigations to validate the provisional diagnosis. After reviewing the results of additional tests for confirming the diagnosis the best course of treatment is decided. The outcome of treatment is monitored at every stage during the period of hospital stay and if the patient's condition is contrary to expected prognosis, other causes and exacerbating factors are investigated.

Outpatient records are single page forms to capture brief clinical notes, routine test results and prescriptions in a simplified manner, designed to describe conditions not requiring hospitalization. When a patient is treated as outpatient and inpatient, both sets of records should be seamlessly integrated datewise.

Even though IT obviates the need for paper records certain documents like referral notes or consent letter should be preserved for medical audit and medicolegal purposes.

Clinical diagnostics and lab investigations yield numeric results which can be easily computerized. Many equipment have provision to directly transfer data on to PCs and printout formatted reports. Software used for lab automation can receive online request for test, prepare priority queue for equipment and task list for staff, schedule specimen collection, assign unique identification number and print labels or tags, prepare checklist for each test, capture data, store it in EMR or send by e-mail/SMS, compare with normal range, detect trends in a patient over a period, identify equipment variability for recalibration and determine specimen sampling size for research. Some software also feature animated demonstrations and instruction about laboratory procedures for the benefit of inexperienced staff.

Digital Library and Information on the Web

Documentation of advances in medical knowledge is necessary to update skill and be aware of latest practices. A wide array of textbooks, journals, CME tutorials, monographs and other medical literature is available in CD-ROM and DVD formats. The advantages of digital documents over printed books are less price, convenient size, better quality content, pick and choose kind of presentation, quick search, automatic indexing and cross-referencing (hyperlinks) and personalized utilities for dictionary look up, annotation and book marking. The embedded audio and video clips makes for interesting and realistic look and feel while reading the text. MEDLINE and MEDLARS are online medical information search services that collect information from a wide variety of national and international medical journals and service subscriber requests. Medical Subject Heading (MeSH) is a database of subject index which makes this search easier. Untrained users are sometimes frustrated by the large lists produced by simple searches. Using MeSH terms in conjunction with Boolean text—words, limits for search and qualifiers for sorting refines the search process.

Except for regular medical practice or using familiar software, any other serious minded pursuit represents considerable time for learning new software and investment in new gadgets. The world wide web provides and opportunity to make best use of this training and investment. The backbone or the permanently dedicated resources of the internet consists of very powerful servers open for global access and maintained by US Department of Defence, European Academic Research Network, few educational and commercial networks like Telenet, JANET and CompuServ. Since the ownership of internet transcends boundaries the issues related to governance are managed by a multilateral body—Internet Governance Forum. The www is a vast repository of information, updated with new information every second, which in principle is accessible to anyone in the world through a telephone line. Websites are hosted by commercial network (.net) governments (.gov), commercial business (.com), not for profit organizations (.org) and educational institutions (.edu). There are also content providers with less well known website suffixes like .biz, .ac and country based ones. Internet browsing refers to

searching for information containing key words, then viewing the list of headings and titles tagged to the key word and finally clicking the links to see the web page, abstract or find the homepage of the appropriate website. If the content is useful then we can download to our computer. There are both free downloadable sites and 'pay to use' sites. The simplest way to pay online is to use credit cards through payment gateway services. Payment gateways are secure websites that ensure fraud free and confidential cash transaction between buyer and seller. Users should be very careful about providing credit card numbers and other personal identity information to websites without security certificate (e.g. VeriSign SSL) and privacy policy. If one doesn't have valid credit card, they can also notify their bank to electronically fund transfer (EFT) to the bank account of the seller. For this one should know the EFT code of receiving bank. Once fund is transferred the bank sends e-mail with digital signature to both parties confirming the transaction. Many banks offer direct online banking facility whereby users can transact from home or office. A user subscribing to internet services can visit websites, access virtual private networks (VPNs) if authorized, e-mail, join discussion and social networking sites, chat or conference online, send and receive files and do business transactions through secure web applications.

DECISION SUPPORT AND EXPERT SYSTEMS

Software is increasingly used to help in decision making within a very small domain of knowledge. They use algorithm which is a simple step by step decision making process which can be repeated (thousands of times) with a different dependent variable each time, to solve a complex real life problem. The simplest method to mimic human thinking is by data mining or recognizing patterns in the historical records. When the database is sufficiently large the system can be quizzed to list cause and effect relationship with a degree of probability that is acceptable. Other artificial intelligence algorithms use artificial neural networks and fuzzy logic framework.

The earliest application of expert systems in medicine was the clinical history questionnaire. Collection of patient data is prone to errors and distortions because of the subjective nature of patient-doctor relationship. Besides, the consultation interview and physical examination may fall short of the optimum scientific standards. Using computer displayed standard questionnaire, patients can answer questions regarding family history, symptoms, lifestyle and habits and past medications in the privacy and comfort, without being probed by the doctor. From this a flow chart approach to evaluate the patient's response can lead to a fairly good differential diagnosis. More advanced software can combine this data with demographic profile, susceptibility factors, predisposing risks and latest research findings to narrow down the list and suggest further investigation.

Most of the expert systems developed for diagnosis and monitoring therapy have demonstrated the concept of clinical decision making based on quantitative and qualitative data, without being available commercially. One of the earliest projects carried out in 1977 at University of Southern California was the Digitalis Therapy Adviser. This expert system monitored the cardiac functions, renal functions and serum drug levels during therapy to reduce the incidence of toxicity. MYCIN developed at Stanford University assists medical students with diagnosis and treatment of wide range of infections. AI/RHEUM contains a structured knowledge based diagnosis criteria for 26 rheumatologic diseases, designed by specialists for general physicians. It was developed and tested at University of Missouri, Columbia and gave the correct diagnosis in 94% of the cases.

Since expert systems require collaboration of many experienced clinicians, computer program mers and extensive trials, only few solutions that were first released in the 80s are in popular use today.

CONTINUING MEDICAL EDUCATION AND COLLABORATION

With good IT infrastructure, learning methods based on CDs and websites are less expensive than classroom lectures. It is also self-paced so that medical knowledge transfer progresses according to the learning curve (ability) of the individual. ADAMS is a software for screen based teaching of anatomy without specimens, cadaver or actual dissection. ADAMS features organ systems, tissues and body structure with 3-D rotation and zoom views. It incorporates biomechanics during body movement and anatomical changes due to several

pathological conditions. Latest version of ADAMS includes thin slice CT and MRI images of normal males and females from head to toe. This software has interactive voice instructor and a dissection practice console that simulates a cadaver dummy on which the student can trace the incision line with mouse or stylus on touch screen.

Today many workshops and hands on training sessions are beamed worldwide as live video over broadband internet (web cast). Web seminars and Web conferencing help medical graduates and practitioners participate in the academic programs offered by centers of excellence. In future, health care networks will invest in telemedicine to take superspecialty services to remote places.

Projects involving multicenter research collaborations are better managed by sharing clinical data and periodic review. Epi Info is a public domain statistical analysis software for epidemiology developed by CDC, Atlanta, USA. Researchers can use it to validate questionnaires, capture data and analyze. It can be freely downloaded from official WHO website.

With more and more IT getting integrated into medical science and practice, it is important for doctors to know about its applications and benefits. Table 59.1 gives the common applications in medicine which can be easily implemented by off the shelf, competitively priced solutions.

Table 59.1: Application of IT in health care systems

Task	*Type of software/IT system required*
Accounting/financial affairs	Spreadsheet Business management software Medical practice administration system
Calendar/contacts/diary	Personal information manager *Microsoft outlook, Kontact, Lotus Organizer, Plaxo*
Clinical coding	Clinical audit information system *Read codes, ICD-10, SNOMED-CT (NHS guidelines)*
Communicating with colleagues	E-mail, Internet telephony—Voice and video, web conferencing and video conference facility for live discussion
CME, computer assisted learning	CD-ROM based tutors and quiz Online services, e-journals and discussion groups Online services for interactive classroom and self-evaluation
Diagnosis	Diagnostic expert systems, e.g. *MYCIN, DXplain, VisualDX*
Decision about treatment	Therapeutic decision support software, e.g. Cochrane database, digitalis therapy adviser Adverse drug reaction monitors, e.g. Lexi-Comp Interact, GeneMedRx
Electronic medical records	Dedicated EMR systems complying with all standards
Illustrations/diagrams/ graphics/audio visual	Microsoft paint, Adobe Illustrator, CorelDraw Photo, graphics editing software Multimedia player and editing software
Medical imaging	Specialized imaging systems
Patient education	Customized websites and audiovisual presentation in local language
Planning interventional therapy and surgery	Dedicated planning systems for interventions and radiotherapy Virtual reality systems for surgical simulation
Practice administration	Clinic or hospital work flow automation solution interfaced with EMR
Presentation slides and publications	Presentation software, e.g. *Microsoft power point* Desk top publishing (DTP) system Bibliographic/literature management software, *e.g. End Note Plus, PubMed* Medical Information Search—MEDLINE, Novoseek
Quality audit for labs, medical care and nonclinical services	Standard operating process document repository, track and trace systems to monitor accuracy, reliability and service levels of patient care
Research data collection and statistical analysis	Spread-sheets and database statistical software, e.g. *Microsoft excel, SPSS, Pro-Stat, Epi Info*
Telemedicine and distance learning	Video conferencing facility. CD or Online library of high quality pictures, images and video clips CD or Online Medical Dictionary
Writing letters, medical reports, papers/articles, CVs, leaflets, information handouts and teaching materials	Word processor, DTP and presentation software

(*Source:* 'Medicine and the Internet', Bruce C McKenzie (Eds), 2nd edition, 1999, OUP)

GLOSSARY

Application	Software that manages a user task and not the computer hardware
Archive	Files stored in back up disks and not in currently used (live) database
ASCII	American standard code for information interchange
Attachment	A file attached along with e-mail. For secure transmission of large files FTP is recommended
Bandwidth	The maximum data communication capacity in Mega or Giga Bits Per Second (MBPS/GBPS) of a network connection. Applications that communicate using local cable or dedicated WAN communication have very high bandwidth. Applications that communicate using shared cable or Internet have much less bandwidth.
Boolean logic	Used to define search criteria when using indexed databases such as MEDLINE. AND, NOT and OR are Boolean operators, used to narrow the search, e.g. 'Find asthma NOT occupational' or 'Find asthma OR occupational lung' or 'Find asthma AND allergic'.
Bugs	Error in system or software
CD-ROM/DVD	Compact disk read only memory/ digital versatile disk
Chat	Two way instant messaging
Database	Data stored in a systematic, easy to identify and retrieve format
Digital signature	A service provided by trusted sites to authenticate the communication send between two secure addresses connected through internet
DNS	Domain name system is a easy to remember name, word or phrase that can be substituted in place of internet address.
EMR	Electronic medical records
File compression	Compressing the file size without loss of information. Usually compressed files are used for sending and receiving over the internet. It is decompressed before user opens, edits or updates and saves the file.
File encryption	Files and information send through internet or public networks can be converted to secret codes so that anyone viewing or copying illegally will not be able to read the original message. It is decrypted by authorized recipient before using.
FTP	File transfer protocol is a special service provided by free or paid sites for authorized persons to upload and download important and confidential files without risk of public disclosure or corruption.
HISA	Health informatics service architecture
HR	Human resources system
HTML/XML	Hypertext markup language/Extended markup language
ICT	Information and communications technology
Internet address	Every connection on the internet is identified by internet protocol address or uniform resource locator such as 158.152.64.237
Intranet	A wide area private network that shares internet communication resources
Mac	Apple macintosh operating system
MMS	Multimedia messaging service
Netiquette	A code of conduct and simple, polite writing style expected of users especially when posting messages to mail and discussion groups.
Network traffic	The total number of users, devices, medical equipment and online applications sending and receiving data through network cables (or wireless modems)
PC	IBM compatible personal computers
SQL	Structured query language
TCP/IP	Transmission control protocol/internet protocol

USB	Universal serial bus
Video conference	Online conference between people in different locations by two way real time communication of video, sound, computer and any other signals.
VPN	Virtual private network

Appendix

SERUM—NORMAL VALUES

Acetoacetate	0.3-2.0 mg/dL
Acid phosphatase	0-0.8 U/mL
Acid phosphatase, prostatic	2.5-12.0 IU/liter
Albumin	3.0-5.5 g/dL
Aldolase	1-6 IU/liter
Alkaline phosphatase	
15-20 years	40-200 IU/liter
above 20 years	35-125 IU/liter
Alpha-1 antitrypsin	200-500 mg/dL
Ammonia	11-35 mmol/liter
Amylase, serum	2-20 U/liter
Anion gap	8-12 mEq/liter (mmol/liter)
Bilirubin	
Total	0.2-1.2 mg/dL
Direct	0-0.4 mg/dL
Bromsulphalein (BSP)	
Normal retention	0.5% at 45 min
Calcium, serum	8.7-10.6 mg/dL
Carbon dioxide, total	18-30 mEq/liter (mmol/liter)
Carotene (carotenoids)	50-300 μg/dL
C3 complement	55-120 mg/dL
C4 complement	14-51 mg/dL
Ceruloplasmin	15-60 mg/dL
Chloride, serum	95-105 mEq/liter (mmol/liter)
Cholesterol, total	
12-19 years	120-230 mg/dL
20-29 years	120-240 mg/dL
30-39 years	140-270 mg/dL
40-49 years	150-310 mg/dL
50-59 years	160-330 mg/dL
	} 50-60 percent as esters
Copper	100-200 μg/dL
Creatine phosphokinase, total	20-200 IU/liter
Creatine phosphokinase, isoenzymes	
MM fraction	94-95%
MB fraction	0-5%
BB fraction	0-2%
Normal values in	
Heart	80% MM, 20% MB
Brain	100% BB
Skeletal muscle	95% MM, 2% MB

Creatinine, serum	
Female adult	0.5-1.3 mg/dL
Male adult	0.7-1.5 mg/dL
Folate, serum	1.9-14.0 ng/mL
Gamma-glutamyl transpeptidase	
Male	12-38 IU/liter
Female	9-31 IU/liter
Gastrin	60-200 pg/mL
Glucose, serum	70-120 mg/dL
Glucose 6-phosphate dehydrogenase	5-10 IU/g Hb
G-6-PD screen, qualitative	Negative
Haptoglobin	100-300 mg/dL
Hemoglobin A_2	0.4% of total Hb
Hemoglobin F	0-2% of total Hb
Immunoglobulin, quantitation	
IgG	700-1500 mg/dL
IgA	70-400 mg/dL
IgM	
Male	30-250 mg/dL
Female	30-300 mg/dL
IgD	0-40 mg/dL
Insulin, fasting	6-26 μU/mL
Iron binding capacity	250-400 μg/dL
Iron, total, serum	40-150 μg/dL
Iodine	3-6.5 μg/dL
Iodine protein bound	4-8 μg/dL
Lactic acid	0.6-1.8 mEq/liter
LDH, serum	20-220 IU/liter
LDH isoenzymes	
LDH_1	20-34%
LDH_2	28-41%
LDH_3	15-25%
LDH_4	3-12%
LDH_5	6-15%
Leucine aminopeptidase (LAP)	30-55 IU/liter
Lipase	4-24 IU/dL
Magnesium, serum	1.5-2.5 mEq/liter
5'-Nucleotidase	0.3-3.2 Bodansky units
Osmolality, serum	278-305 mOsm/kg serum water
Phenolsulfonphthalein (PSP)	>25% excreted within 15 minutes after injection of 1 mL dye
Phenylalanine	3 mg/dL
Phosphorus, inorganic, serum	2.0-4.3 mg/dL
Potassium, plasma	3.1-4.3 mEq/liter
Potassium, serum	3.5-5.2 mEq/liter
Protein, total, serum	
2-55 years	5.0-8.0 g/dL
Above 55 years	6.0-8.3 g/dL

Protein electrophoresis serum	
Albumin	3.2-5.2 g/dL
Globulin: Alpha-1	0.6-1.0 g/dL
Globulin: Alpha-2	0.6-1.0 g/dL
Globulin: Beta	0.6-1.2 g/dL
Globulin: Gamma	0.7-1.5 g/dL
SGOT	5-40 IU/liter
SGPT (ALT)	5-30 IU/liter
Sodium, serum	135-145 mEq/liter
Sulfate	0.5-1.5 mg/dL
T_3 uptake	25-45%
T_4	4.5-11.5 μg/dL
Triglycerides	
2-29 years	10-140 mg/dL
30-39 years	20-150 mg/dL
40-49 years	20-160 mg/dL
50-59 years	20-190 mg/dL
Above 60 years	20-200 mg/dL
Total lipids	500-600 mg/dL
Urea nitrogen, serum	
2-65 years	5-22 mg/dL
Above 65 years	
Male	10-38 mg/dL
Female	8-26 mg/dL
Uric acid	
10-59 years	
Male	2.5-9.0 mg/dL
Female	2.0-8.0 mg/dL
Above 60 years	
Male	2.5-9.0 mg/dL
Female	2.5-9.0 mg/dL
Viscosity	1.4-1.8 (serum compared to H_2O)
Vitamin A	0.15-0.60 μg/mL
Vitamin B_{12}	200-850 pg/mL

URINE—NORMAL VALUES

Acidity, titratable	20-40 mEq/24 h
Ammonia	30-50 mEq/24 h
Amylase	35-260 Somogyi units/h
Bence-Jones protein	Negative
Bilirubin	Negative
Calcium	
Normal diet	0.5-0.31 mEq/kg body weight/24 h
Low calcium diet (200 mg/day)	< 150 mg/24 h
Chloride	120-240 mEq/24 h (varies with dietary intake)
Copper	0-32 µgn/24 h

Creatine	
Male	0-40 mg/24 h
Female	0-100 mg/24 h
Creatinine	1.0-1.6 g/24 h or 15-25 mg/kg body weight/24 h
Cysteine, qualitative	Negative
Glucose,	
qualitative	Negative
quantitative	16-300 mg/24 h
Iron	40-140 μg/24 h
Lead	0-120 μg/24 h
Osmolality	50-1200 mOsm/kg
pH	4.6-8.0
Phosphorus	0.8-2.0 g/24 h
Porphobilinogen	
qualitative	Negative
quantitative	0-2.4 mg/24 h
Porphyrin	
Coproporphyrin	50-250 μg/24 h
Uroporphyrin	10-30 μg/24 h
Potassium	25-100 mEq/24h
Protein	
qualitative	Negative
quantitative	10-150 mg/24 h
Sodium	130-260 mEq/24 h (varies with dietary sodium intake)
Specific gravity	1.003-1.030
Uric acid	80-976 mg/24 h
Urobilinogen	0.05-3.5 mg/24 h < 1.0 Ehrlich units/24 h

HEMATOLOGIC—VALUES

Bone marrow, differential cell count	
Myeloid cells	56.7%
Neutrophilic series	53.6%
Myeloblasts	0.3-5.0%
Promyelocytes	1-8%
Myelocytes	5-19%
Metamyelocytes	9-24%
Bands	9-15%
Segmented cells	7-30%
Eosinophil precursors	0.5-3.0%
Eosinophils	0.5-4.0%
Basophilic series	0.2-0.7%
Erythroid series	20-30%
Erythroid cells in bone marrow	
Pronormoblasts	1-8%

Basophilic normoblasts Polychromatophilic normoblasts Orthochromatic normoblasts	7-32%
Megakaryocytes in bone marrow	0.1%
Lymphoreticular cells	
Lymphocytes	3-17%
Plasma cells	0-2%
Reticulum cells	0.1-2.0%
Monocytes	0.5-5%
Myeloid/erythroid ratio	3:1 to 4:1
Carboxyhemoglobin	
Nonsmoker	0-2.3%
Smoker	2.1-4.2%
Folate, RBC	120-670 ng/mL
Fragility, osmotic	
Hemolysis begins	0.45-0.38% NaCl
Hemolysis completed	0.33-0.30% NaCl
Haptoglobin, serum	100-300 mg/dL
Hemochromogens, plasma	3-5 mg/dL
Methemoglobin	<1.8%
Reticulocyte count	25,000-75,000/mm^3 or 0.5-2.0% of erythrocyte count

Volume

	Male	Female
Blood	52-83 mL/kg	50-75 mL/kg
Plasma	25-43 mL/kg	28-45 mL/kg
Red cell	20-36 mL/kg	19-31 mL/kg

COAGULATION—NORMAL VALUES

Bleeding time	
Duke	1-4 min
Ivy	1-9 min
Clot retraction, qualitative	Apparent in 30-60 min, complete in 24 h, usually in 6 h
Coagulation time (Lee-White)	
Glass tubes	5-15 min
Siliconized tubes	20-60 min
Euglobulin lysis time	120-240 min
Fibrin degradation product	< 10 μg/mL or titer < 1.4
Fibrinogen	200-400 mg/dL
Partial thromboplastin time (PTT)	
Standard technique	68-82 sec
Activated	24-38 sec
Prothrombin time (PT)	11-14 sec
Thrombin time	10-15 sec
Whole blood clot lysis time	> 24 h

Reticulocyte Index Correction Factor

Hematocrit	Correction factor
45	1.00
40	0.71
35	0.52
30	0.38
25	0.28
20	0.20
15	0.13

Note: Reticulocyte index = Percent retriculocytes × correction factor for hematocrit and early bone marrow release.

CEREBROSPINAL FLUID—NORMAL VALUES

Bilirubin	0
Cells	0-5/mm^3, all lymphocytes
Chloride	110-129 mEq/liter
Glucose	48-86 mg/dL or >60% of serum glucose
pH	7.31-7.43
Pressure	7-20 cm water
Protein, lumbar CSF	15-45 mg/dL
Albumin	58%
Alpha-1	9%
Alpha-2	8%
Beta	10%
Gamma	10% (5-12)
Protein, cisternal CSF	15-25 mg/dL
Protein, ventricular CSF	5-15 mg/dL

GASTROINTESTINAL AND LIVER FUNCTION TESTS

Absorption

D-xylose absorption (25 g D-xylose orally after an 8 h fast, urine collected for 5 h following ingestion)	
Urinary excretion	> 5 g/5 h
Serum (1 h after ingestion)	> 25 mg/dL
Vitamin A (200,000 U vitamin A orally; serum level obtained 5 h after ingestion)	> twice fasting vitamin A level

Hepatic function

Bromosulphalein (BSP) test (5 mg/kg BSP intravenously: serum level 45 minutes later)	< 5% retention at 45 min

Secretion

Gastric secretion	
Volume (mean ± standard deviation)	
Basal, fasting	
Male	64 ± 21 mL/h
Female	54 ± 24 mL/h
Maximally stimulated (after 0.004 mg histamine/kg body weight, subcutaneously)	
Male	201 ± 53 mL/h
Female	153 ± 33 mL/h
Acid output (mean ± standard deviation)	
Basal, fasting (BAO)	
Male	3.7 ± 2.1 mEq/h
Female	2.2 ± 1.7 mEq/h
Maximal stimulated output/mt (MAO) (after 0.004 mg histamine/kg body weight, subcutaneously)	
Male	23 ± 7 mEq/h
Female	18 ± 5 mEq/h
Basal acid output/maximal acid output ratio	<0.6

Pancreatic secretion

Basal	
Bicarbonate	25-150 mEq/h
pH	7.5-8.8
Volume	1-99 mL/h
Secretion stimulated (2 unit secretin per kg body weight, intravenously)	
Bicarbonate	60-90 mEq/liter
Volume	38-314 mL/h

SEMEN—NORMAL VALUES

Volume	2.0-6.6 mL
Spermatocyte count	>50 million/mL
Liquefaction	Complete in 15 min
Morphology of sperms	>60% normal forms
Motility	>75% activity motile
pH	7.2-8.0
Spermatocrit	10%

SYNOVIAL FLUID—NORMAL VALUES

Cells	<200 cells mm^3
Polymorphonuclear	<25%
Crystals	None
Fibrin clot	None
Glucose	Same as serum

Hyaluronic acid	2.45-3.97 g/dL
pH	7.31-7.64
Protein	<2.5 g/dL
Albumin	63%
α_1-globulin	7%
α_2-globulin	7%
β-globulin	9%
γ-globulin	14%
Relative viscosity	>300
Uric acid	Same as serum

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